This compound was prepared by General Method 8 (EXAMPLE 238) from Carbostyril 124 (structure **56** of **Scheme XVI**, where R^1=R^2=H, R^3=methyl, Y=NH) (500 mg, 2.8 mmol) to afford 175 mg (25%) of Compound **241** as a pale yellow solid. Data for Compound **241**: mp 282-284 °C; **IR** (KBr, cm^{-1}) 2966, 2918, 1658, 1641, 1425, 1257; **^{1}H NMR** (400 MHz, $CDCl_3$) 7.24 (s, 1 H), 6.34 (s, 1 H), 6.23 (s, 1 H), 5.37 (s, 1 H), 2.41 (s, 3 H), 2.04 (s, 3 H), 1.29 (s, 6 H); **^{13}C NMR** (100 MHz, $CDCl_3$) 165.0, 149.8, 146.5, 140.3, 129.2, 127.6, 119.1, 118.5, 114.9, 112.5, 97.2, 52.4, 31.8, 19.3, 18.9.

EXAMPLE 142

1,2-Dihydro-10-hydroxy-2,2,4-trimethyl-10*H*-isochromeno[4,3-*g*]quinoline (Compound **242**, structure **62** of **Scheme XVI**, where R^1=H, R^2=R^3=benzo, Y=O)

To a yellow solution of Compound **239** (EXAMPLE 139) (10 mg, 0.033 mmol) in 0.5 mL of toluene at -78 °C was added 0.050 mL of DIBALH (1.5 M in toluene , 0.075 mmol), and the resulting solution was stirred at -50 ± 10 °C for 20 min. The reaction was quenched with water (1 mL) and extracted with ethyl acetate (2 x 5 mL). Removal of solvent and chromatography of the crude residue (silica gel, 20% ethyl acetate/hexanes) afforded 6 mg (63%) of Compound **242** as a colorless oil. Data for Compound **242**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.74 (d, *J* = 7.8, 1 H), 7.52 (s, 1 H), 7.37 (t, *J* = 7.8, 1 H), 7.31 (d, *J* = 7.8, 1 H), 7.19 (t, *J* = 7.8, 1 H), 6.26 (d, *J* = 6.5, 1 H), 6.17 (s, 1 H), 5.97 (d, *J* = 6.5, 1 H), 5.40 (br s, 1 H), 5.29 (s, 1 H), 2.05 (s, 3 H), 1.27 (s, 6 H).

EXAMPLE 143

1, 2-Dihydro-2,2,4,6-tetramethyl-8*H*-pyrano[3,2-*g*]quinoline (Compound **243**, structure **61** of **Scheme XVI**, where R^1=R^2=H, R^3=methyl, Y=O)

1,2-Dihydro-2,2,4,6-tetramethyl-8-pyranono[5,6-*g*]quinoline (structure **57** of **Scheme XVI**, where R^1=R^2=H, R^3=methyl, Y=O) To a solution of 7-nitro-4-methylcoumarin (structure **55** of **Scheme XVI**, where R^1=R^2=H, R^3=methyl, Y=O) (0.61 g, 1.75 mmol) was added 50 mg of 10% Pd/C. The reaction mixture was stirred under an atmosphere of H_2 for 2 h. The mixture was filtered through a pad of Celite™ and the filtrate was concentrated to give 0.5 g of the crude amino compound as a yellow solid. This material was used without further purification, and was submitted to General Method 3 to afford 90 mg (20%) of 1,2-dihydro-

2,2,4,6-tetramethyl-8-pyranono[5,6-*g*]quinoline as a yellow solid. Data for 1,2-dihydro-2,2,4,6-tetramethyl-8-pyranono[5,6-*g*]quinoline: mp 258-260 °C; **IR** (KBr) 3300, 2955, 1720, 1630, 1505, 1390, 1250; **^{1}H NMR** (400 MHz, $CDCl_3$) 7.27 (s, 1 H), 6.30 (s, 1 H), 6.12 (br s, 1 H), 5.84 (s, 1 H), 5.44 (s, 1 H), 2.37 (s, 3 H), 2.05 (s, 3 H), 1.32 (s, 6 H); **^{13}C NMR** (100 MHz, $CDCl_3$) 161.9, 155.4, 153.1, 147.1, 128.8, 127.0, 119.2, 110.3, 109.0, 98.6, 52.6, 31.8, 18.6.

1, 2-Dihydro-2,2,4,6-tetramethyl-8*H*-pyrano[3,2-*g*]quinoline (Compound **243**, structure **61** of **Scheme XVI**, where R^1=R^2=H, R^3=methyl, Y=O) To a solution of 1,2-dihydro-2,2,4,6-tetramethyl-8-pyranono[5,6-*g*]quinoline (15 mg, 0.06 mmol) in 1 mL of toluene at -78°C was added DIBA1-H (0.5 M in toluene, 0.24 mL, 0.12 mmol) and the resulting mixture was allowed to stir at -50°C for 60 min, generating a clear brown solution. The reaction was quenched with water (1 mL) and was extracted with ethyl acetate (2 x 10 mL). The organic extract was concentrated and was chromatographed (silica gel, 4:1 hexanes /ethyl acetate) to afford 1 mg (5%) of Compound **243** as a colorless oil. Data for Compound **243**: **^{1}H NMR** (400 MHz, acetone-d_6) 6.84 (s, 1 H), 5.96 (s, 1 H), 5.33 (t, *J* = 3.5, 1 H), 5.26 (s, 1 H), 5.21 (s, 1 H), 4.59 (d, *J* = 3.5, 2 H), 1.96 (s, 3 H), 1.93 (s, 3 H), 1.24 (s, 6 H).

EXAMPLE 144

(*R/S*)-1,2,3,4-Tetrahydro-2,2,4-trimethyl-10-isoquinolono[4,3-*g*]quinoline (Compound **244**, structure **63** of **Scheme XVI**, where R^1=H, R^2=R^3=benzo, Y=O) Hydrogenation of Compound **240** (550 mg, 1.9 mmol) over 10% Pd/C (200 mg) in 250 mL of ethyl acetate for 14 h at rt afforded 510 mg (92%) of Compound **244** as a yellow solid. Data for Compound **244**: mp 263-264 °C; **IR** (KBr) 3304, 2960, 2928, 1658, 1606, 1467, 1267 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) 9.67 (br s, 1 H), 8.45 (d, *J* = 8.0, 1 H), 8.11 (d, *J* = 8.0, 1 H), 7.94 (s, 1 H), 7.69 (t, *J* = 8.0, 1 H), 7.41 (t, *J* = 8.0, 1 H), 6.25 (s, 1 H), 4.08 (br s, 1 H), 3.02 (m, 1 H), 1.81 (dd, *J* = 12.8, 5.2, 1 H), 1.49 (t, *J* = 12.8, 1 H), 1.46 (d, *J* = 6.7, 3 H), 1.29 (s, 3 H) and 1.23 (s, 3 H).

EXAMPLE 145

1,2-Dihydro-2,2,4-trimethyl-10-thioïsoquinolono[4,3-*g*]quinoline (Compound **245**, structure **58** of **Scheme XVI**, where R^1=H, R^2=R^3=benzo, Y=O)

A mixture of Compound **240** (9 mg, 0.03 mmol) and Lawesson's reagent (41 mg, 0.1 mmol) in 2 mL of THF was stirred at 80°C for 3 h, generating a bright yellow solution. Removal of the solvent and chromatography of the crude mixture (silica gel, 1:1 ethyl acetate/hexanes) afforded 8.2 mg (90%) of Compound **245** as a yellow oil. Data for Compound **245**: **^{1}H NMR** (400 MHz, acetone-d_6) 8.93 (d, *J* = 8.1, 1 H), 8.33 (d, *J* = 8.1, 1 H), 8.01 (s, 1 H), 7.75 (t, *J* = 8.1, 1 H), 7.44 (t, *J* = 8.1, 1 H), 6.73 (s, 1 H), 5.97 (br s, 1 H), 5.51 (s, 1 H), 2.15 (s, 3 H), 1.35 (s, 6H).

EXAMPLE 146

(+)-1,2,3,4-Tetrahydro-2,2,4-trimethyl-10-isoquinolono[4,3-*g*]quinoline (Compound **246**, structure **63** of **Scheme XVI**, where R^1=H, R^2=R^3=benzo, Y=O)

This compound was prepared by a HPLC separation of the enantiomers of Compound **244** using a Chiracel OD-R column, using a 4:1 mixture of methanol and water as the mobile phase. The optical purity of Compound **246** was determined by HPLC to be > 99% e.e.; $[\alpha]^{20}_D = +106$ (MeOH).

EXAMPLE 147

1,2-Dihydro-2,2,4-trimethyl-6-trifluoromethyl-8-pyridono[5,6-*g*]quinoline (Compound **247**, structure **57** of **Scheme XVII**, where R^1=R^2=H, R^3=trifluoromethyl, Y=NH) This compound was prepared as depicted in **Scheme XVII** and as described below.

1-*tert*-Butyloxycarbamoyl-3-nitrobenzene (structure **65** of **Scheme XVII**, whereR^1=H, P=*t*-butyloxycarbonyl, Y=NH). General Method 10. *N*-Boc-Protection of Nitroanilines To a flame-dried 500 mL r.b. flask containing 3-nitroaniline (structure **64** of **Scheme XVII**, where R^1=H, Y=NH) (20.0 g, 144.8 mmol) in 150 mL THF was added di-*tert*-butyl dicarbonate (31.60 g, 144.8 mmol, 1.00 equivuiv), and the mixture was cooled to 0°C. 4-*N*,*N*-Dimethylaminopyridine (19.46 g, 159.3 mmol, 1.10 equivuiv) was added portion-wise, and the mixture was allowed to warm to rt overnight. Ethyl acetate (400 mL) was added, and the mixture was washed with 1M $NaHSO_4$(aq) (2 x 200 mL) and brine (200 mL), dried

(Na_2SO_4), and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, hexanes/ethyl acetate, 9:1) afforded 31.4 g (91%) of 1-*tert*-butyloxycarbamoyl-3-nitrobenzene as a white solid. Data for 1-*tert*-butyloxycarbamoyl-3-nitrobenzene: **^{1}H NMR** (400 MHz, $CDCl_3$) 8.31 (dd, 1H, J = 2.2, 2.2, 1H, 2-H), 7.88 (dd, J = 7.9, 1.5, 1H, 4-H), 7.69 (br d, $J \approx 7.8$, 1H, 6-H), 7.44 (dd, J = 8.3, 8.1, 1H, 5-H), 6.74 (br s, 1H, N*H*), 1.54 [s, 9H, $(CH_3)_3CO$)].

3-*tert*-Butyloxycarbamoylaniline (structure **66** of **Scheme XVII**, whereR^1=H, P=*t*-butyloxycarbonyl, Y=NH) To an oven-dried 1-L r.b. flask containing 1-*tert*-butyloxycarbamoyl-3-nitrobenzene (20.0 g, 83.9 mmol) in 500 mL 1:1 ethyl acetate/ethanol at rt was added 10% Pd on C (approx 1 mol%), and the mixture was stirred under an atmosphere of H_2 gas for 6 h. The reaction mixture was then filtered, and concentrated under diminished pressure to give 17.4 g (quant of 3-*tert*-butyloxycarbamoylaniline as a white oily solid. Data for 3-*tert*-butyloxycarbamoylaniline: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.04 (t, J = 8.0, 8.0, 1H, 5-H), 6.98 (br s, 1H, N*H*), 6.53 (dd, J = 7.9, 1.8, 1H, 4-H), 6.36 (m, 2H, 6,2-H), 3.66 (br s, 2H, NH_2), 1.51 [s, 9H, $(CH_3)_3CO$)].

7-*tert*-Butyloxycarbamoyl-1,2-dihydro-2,2,4-trimethylquinoline (structure **67** of **Scheme XVII**, whereR^1=H, P=*t*-butyloxycarbonyl, Y=NH) General Method 11: Skraup Cyclization of *tert*-Butyloxycarbamoylanilines To an oven-dried 1 L r.b. flask containing 3-*tert*-butyloxycarbamoylaniline (17.4 g, 83.5 mmol), $MgSO_4$ (50 g, 5 equivuiv), and 4-*tert*-butylcatechol (420 mg, 3 mol%) in 120 mL acetone (approx 0.75 M in the aniline) was added iodine (1.07 g, 5 mol%), and the mixture was heated to reflux for 8 h. The crude reaction mixture was then cooled to rt, filtered through a bed of Celite™ on a fritted-glass funnel, rinsing with ethyl acetate, dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, hexanes/ethyl acetate, gradient elution) afforded 19.9 g (82%) of 7-*tert*-butyloxycarbamoyl-1,2-dihydro-2,2,4-trimethylquinoline as a white solid, which was further purified by recrystallization from acetonitrile to give white needles. Data for 7-*tert*-butyloxycarbamoyl-1,2-dihydro-2,2,4-trimethylquinoline: **^{1}H NMR** (400 MHz, $CDCl_3$) 6.93 (d, J = 8.3, 1H, 5-H), 6.81 (br s, 1H, *H*NBoc), 6.34 (m, 2H, 6,8-H), 5.21 (d, *J* = 0.9, 1H, 3-H), 3.71 (br s, 1H, N*H*), 1.94 (d, *J* = 1.0, 3H, 4-CH_3), 1.50 [s, 9H, $(CH_3)_3CO)$], 1.24 [s, 6H, 2-$(CH_3)_2$].

7-Amino-1,2-dihydro-2,2,4-trimethylquinoline General Method 12: Removal of Boc Protective Group from Compounds of structure **67** of **Scheme XVII**, where P=*t*-butyloxycarbonyl, Y=NH) To an oven-dried 25 mL r.b. flask containing 7-*tert*-butyloxycarbamoyl-1,2-dihydro-2,2,4-trimethylquinoline (400 mg, 1.38 mmol) in 2 mL dichloromethane at 0°C was added trifluoroacetic acid (1.06 mL, 10 equivuiv), and the mixture was allowed to warm to rt. After 3 h at rt, the reaction mixture was diluted with 50 mL dichloromethane, transferring to a 125 mL erlynmeyer flask, and cooled to 0°C before neutralization to pH 8 with sat'd aqueous $NaHCO_3$. The biphasic mixture was transferred to a separatory funnel, the layers were separated, and the organic phase was dried (Na_2SO_4), and concentrated under reduced pressure to afford a light reddish oil. The crude material thus obtained was of greater than 98% purity by ^1H NMR, and was carried on to the next step without further purification. While the 7-amino-quinoline obtained decomposed appreciably within a few hours upon standing at rt, ethanolic solutions could be stored at -20°C for 2-3 days without substantial adverse effect on the subsequivuent reaction outcome. Typically however, the material was stored in bulk as the crystalline Boc-protected amine, and portions were hydrolysed as needed. Data for 7-amino-1,2-dihydro-2,2,4-trimethylquinoline: **^{1}H NMR** (400 MHz, $CDCl_3$) 6.86 (d, *J* = 8.2, 1H, 5-H), 5.99 (dd, *J* = 8.0, 2.3, 1H, 6-H), 5.79 (d, *J* = 2.0, 1H, 8-H), 5.12 (d, *J* = 1.4, 1H, 3-H), 3.53 (br s, 3H, NH_2, N*H*), 1.93 (d, *J* = 1.2, 3H, 4-CH_3), 1.24 [s, 6H, 2-$(CH_3)_2$].

1,2-Dihydro-2,2,4-trimethyl-6-trifluoromethyl-8-pyridono[5,6-*g*]quinoline (Compound **247**, structure **57** of **Scheme XVII**, where R^1=R^2=H, R^3=trifluoromethyl, Y=NH) General Method 13: Knorr Cyclization of 7-amino-1,2-dihydro-2,2,4-trimethylquinolines with a β-Keto Ester To an oven-dried 10 mL r.b. flask containing 7-amino-1,2-dihydro-2,2,4-trimethylquinoline (100 mg, 0.53 mmol) and ethyl 4,4,4-trifluoroacetoacetate (85.4 mL, 0.58 mmol, 1.1 equivuiv) in 2.5 mL absolute ethanol was added $ZnCl_2$ (110 mg, 0.81 mmol, 1.5 equivuiv) and the mixture was heated to reflux for 3 h. Upon cooling to rt, the reaction mixture was diluted with 40 mL ethyl acetate, and the organic solution was washed with sat'd aqueous NH_4Cl, dried (Na_2SO_4), and concentrated under reduced pressure.

Purification by flash column chromatography (silica gel, hexanes/ethyl acetate, gradient elution) afforded 72 mg (44%) of Compound **247** as a bright fluorescent-yellow solid, in addition to 70 mg (40%) of Compound **248** (EXAMPLE 148) as a pale yellow crystalline solid, and 10.4 mg (6%) of Compound **249** (EXAMPLE 149) as a white solid. Data for Compound **247**: ^{1}**H NMR** (400 MHz, $CDCl_3$) 11.45 (br s, 1H, CON*H*), 7.38 (s, 1H, 5-H), 6.66 (s, 1H, 7-H), 6.27 (s, 1H, 10-H), 5.42 (s, 1H, 3-H), 4.35 [br s, 1H, $(CH_3)_2CNH$], 2.03 (s, 3H, 4-CH_3), 1.33 [s, 6H, 2-$(CH_3)_2$].

EXAMPLE 148

8-Ethoxy-1,2-dihydro-2,2,4-trimethyl-6-trifluoromethyl-8-pyrido[5,6-g]quinoline (Compound **248**, structure **71** of **Scheme XVII**, where $R^1=R^2=H$, R^3=trifluoromethyl, R^5=ethyl, Y=N) This compound was obtained along with Compounds **247** and **249** as described above (EXAMPLE 147). Data for Compound **248**: ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.56 (d, 1H, J = 1.8, 5-H), 6.84 (s, 1H, 7-H), 6.74 (s, 1H, 10-H), 5.52 (s, 1H, 3-H), 4.47 (q, 2H, J = 7.0, CH_3CH_2O), 4.12 [br s, 1H, $(CH_3)_2CNH$], 2.09 (d, 3H, J = 1.3, 4-CH_3), 1.42 (t, 3H, J = 7.0, CH_3CH_2O), 1.34 [s, 6H, 2-$(CH_3)_2$]. This product was readily converted to the 2-quinolone isomer Compound **247** by heating neat with 10 equivuiv *p*-chlorophenol at 180°C for 3 h, giving Compound **247** in >80% yield.

EXAMPLE 149

(*R,S*)-1,2,6,7-Tetrahydro-6-hydroxy-2,2,4-trimethyl-6-trifluoromethyl-8-pyridono[5,6-g]quinoline (Compound **249**, structure **69** of **Scheme XVII**, where $R^1=R^2=H$, R^3=trifluoromethyl, Y=NH) This compound was obtained along with Compounds **247** and **248** as described above (EXAMPLE 147). Data for Compound **249**: ^{1}**H NMR** (400 MHz, DMSO-d_6) 10.16 (s, 1H, CON*H*), 7.09 (s, 1H, 5-H), 6.61 (s, 1H, O*H*), 6.24 (s, 1H, 10-H), 6.01 [s, 1H, $(CH_3)_2CNH$], 5.21 (s, 1H, 3-H), 2.80 and 2.72 (ABq, 2H, J_{AB} = 16.4, 7-H), 1.86 (s, 3H, 4-CH_3), 1.19 and 1.17 [2s, 2 x 3H, 2-$(CH_3)_2$]. This product was readily converted to the 2-quinolone isomer Compound **247** by heating to 60°C in benzene or toluene with a catalytic amount of *p*-TsOH for 2 h, giving Compound **247** in >95% yield.

EXAMPLE 150

(*R/S*)-1,2,3,4-Tetrahydro-2,2,4-trimethyl-6-trifluoromethyl-8-pyranono[5,6-*g*]quinoline (Compound **250**, structure **63** of **Scheme XVIII**, where R^1=R^2=H, R^3=trifluoromethyl, Y=O)

(*R/S*)-1,2,3,4-Tetrahydro-2,2,4-trimethyl-7-(1,1,1-trimethylacetoxy)quinoline (structure **72** of **Scheme XVIII**, where R^1=H, P=*t*-butyl, Y=O) In a dry r.b. flask equivuipped with a magnetic stir bar was suspended 1,2-dihydro-2,2,4-trimethyl-7-(1,1,1-trimethylacetoxy)quinoline (structure **67** of **Scheme XVIII**, where R^1=H, P=*t*-butyl, Y=O; EXAMPLE 138) (1.01 g, 3.37 mmol) and 10% Pd/C (200 mg) in CH_2Cl_2. The flask was charged with H_2 gas and allowed to react for 12h with constant stirring. The suspension was filtered though a bed of Celite™, washed with EtOAc (2 x 50 mL) and concentrated *in vacuo* to afford 996 mg (98%) of (*R/S*)-1,2,3,4-tetrahydro-2,2,4-trimethyl-7-(1,1,1-trimethylacetoxy)quinoline as a light brownish-red solid. Data for (*R/S*)-1,2,3,4-tetrahydro-2,2,4-trimethyl-7-(1,1,1-trimethylacetoxy)quinoline: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.10 (dd, *J* = 8.5, 0.9, 1 H), 6.30 (dd, *J* = 8.4, 2.4, 1 H), 6.13 (d, *J* = 2.2, 1 H), 3.62 (br s, 1 H), 2.87 (m, 1 H), 1.71 (dd, *J* = 13, 5.4, 1 H), 1.41 (apparent t, *J* = 13, 1 H), 1.31 (m, 10 H), 1.22 (s, 3 H), 1.16 (s, 3 H).

(*R/S*)-1,2,3,4-Tetrahydro-7-hydroxy-2,2,4-trimethylquinoline This compound was prepared as described above for 1,2-dihydro-7-hydroxy-2,2,4-trimethylquinoline (EXAMPLE 138) from (*R/S*)-1,2,3,4-tetrahydro-2,2,4-trimethyl-7-(1,1,1-trimethylacetoxy)quinoline (230 mg, 0.845 mmol) to afford (*R/S*)-1,2,3,4-tetrahydro-7-hydroxy-2,2,4-trimethylquinoline, which was used in the following reaction without further purification.

(*R/S*)-1,2,3,4-Tetrahydro-2,2,4-trimethyl-6-trifluoromethyl-8-pyranono[5,6-*g*]quinoline (Compound **250**, structure **63** of **Scheme XVIII**, where R^1=R^2=H, R^3=trifluoromethyl, Y=O) This compound was prepared by General Method 9 (EXAMPLE 238) from crude (*R/S*)-1,2,3,4-tetrahydro-7-hydroxy-2,2,4-trimethylquinoline and ethyl 4,4,4-trifluoroacetoacetate (310 mg, 1.69 mmol, 2 equivuiv) to afford 160 mg (61% overall) of Compound **250** as a yellow solid. Data for Compound **250**: R_f 0.4 (hex/EtOAc, 3:1); **^{1}H NMR** (400 MHz, $CDCl_3$) 7.41 (s, 1 H), 6.37 (s, 1 H), 6.33 (s, 1 H), 4.46 (s, 1 H), 2.92 (m, 1

H), 1.80 (dd, *J* = 13, 5.0, 1 H), 1.42 (dd, *J* = 13, 13, 1 H), 1.38 (d, *J* = 6.0, 3 H), 1.31 (s, 3 H), 1.25 (s, 3 H).

EXAMPLE 151

1,2-Dihydro-2,2,4-trimethyl-6-trifluoromethyl-8-thiopyranono[5,6-*g*]quinoline (Compound **251**, structure **58** of **Scheme XVI**, where R^1=R^2=H, R^3=trifluoromethyl, Y=O) In a dry pressure tube equivuipped with a magnetic stir bar was dissolved Compound **238** (EXAMPLE 138) (50 mg, 0.159 mmol) and Lawesson's reagent (320 mg, 0.79 mmol, 5 equivuiv) in 15 mL toluene. The resulting solution was heated at 100°C for 20 h. The cooled solution was concentrated on Celite ™ to give a free flowing powder which was purified by flash column chromotography (silica gel, hexanes/EtOAc, 5:1) to give 40 mg (78%) of Compound **251** as a bright red solid. Data for Compound **251**: R_f 0.36 (silica gel, hex/EtOAc, 3:1); **^{1}H NMR** (400 MHz, acetone-d_6) 7.25 (s, 1 H,), 4.03 (s, 1 H), 6.89 (br s, 1 H), 6.53 (s, 1 H), 5.62 (s, 1 H), 2.77 (d, *J* = 1.1, 3 H), 1.39 (s, 6 H).

EXAMPLE 152

(*R*/*S*)-1,2,3,4-Tetrahydro-2,2,4-trimethyl-6-trifluoromethyl-8-thiopyranono[5,6-*g*]quinoline (Compound **252**, structure **76** of **Scheme XIX**, where R^1=R^2=H, R^3=trifluoromethyl, Y=O) In a dry pressure tube equivuipped with a magnetic stir bar was dissolved Compound **250** (EXAMPLE 150) (26 mg, 0.0836 mmol) and Lawesson's reagent (60 mg, 0.41 mmol, 5 equivuiv) in 15 mL toluene. The resulting solution was heated at 100°C for 20 h. The cooled solution was concentrated on Celite™ to give a free flowing powder which was purified by flash column chromotography (silica gel, hexanes/EtOAc, 5:1) to afford 19.2 mg (71%) of Compound **252** as a bright orange solid. Data for Compound **252**: Rf 0.37 (silica gel, hex/EtOAc, 3:1); **^{1}H NMR** (400 MHz, $CDCl_3$) 7.43 (s, 1 H), 7.16 (s, 1 H), 6.45 (s, 1 H), 4.59 (br s, 1 H), 2.93 (m, 1 H), 1.82 (dd, *J* = 13, 5.1, 1 H), 1.45 (app t, *J* = 13, 1 H), 1.39 (d, *J* = 6.6, 3 H), 1.34 (s, 3 H), 1.27 (s, 3 H).

EXAMPLE 153

6-Chloro(difluoro)methyl-1,2-dihydro-2,2,4-trimethyl-8-pyranono[5,6-*g*]quinoline (Compound **253**, structure **57** of **Scheme XVII**, where R^1=R^2=H, R^3=chlorodifluoromethyl, Y=O)

This compound was prepared by General Method 9 (EXAMPLE 238) from 1,2-dihydro-7-hydroxy-2,2,4-trimethylquinoline (EXAMPLE 138) (71 mg, 0.37 mmol) and methyl 4-chloro-4,4-difluoroacetoacetate (150 mg, 1.62 mmol, 2.2 equivuiv) to afford 17.6 mg (15 %) of Compound **253** as a light yellow solid. Data for Compound **253**: R_f 0.35 (hex/EtOAc, 3:1); **^{1}H NMR** (400 MHz, $CDCl_3$) 7.40 (s, 1 H), 6.33 (s, 1 H), 6.31 (s, 1 H), 5.41 (s, 1 H), 4.42 (br s, 1 H), 2.02 (s, 3 H), 1.36 (s, 6 H).

EXAMPLE 154

9-Acetyl-1,2-dihydro-2,2,4-trimethyl-6-trifluoromethyl-8-pyridono[5,6-*g*]quinoline (Compound **254**, structure **59** of **Scheme XVI**, where R^1=R^2=H, R^3=trifluoromethyl, R^4=acetyl, Y=N)

To an oven-dried 10-mL r.b. flask containing Compound **247** (15 mg, 0.049 mmol) in 1 mL dichloromethane at rt was added acetic anhydride (0.10 mL, xs) and 4-*N*,*N*-dimethylaminopyridine (6.5 mg, 0.054 mmol, 1.1 equivuiv), and the mixture was stirred 10 min. Dichloromethane (20 mL) was added, and the solution was washed with 1M pH 7 potassium phosphate buffer, dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, hexanes/ethyl acetate, gradient elution) afforded 16 mg (92%) of Compound **254** as a yellow oily solid. Data for Compound **254**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.66 (s, 1H, 5-H), 7.08 (s, 1H, 7-H), 6.83 (s, 1H, 10-H), 5.63 (s, 1H, 3-H), 4.31 [br s, 1H, $(CH_3)_2CNH$], 2.38 (s, 3H, CH_3CON), 2.12 (s, 3H, 4-CH_3), 1.48 [s, 6H, 2-$(CH_3)_2$].

EXAMPLE 155

1,2-Dihydro-2,2,4,10-tetramethyl-6-trifluoromethyl-8-pyridono[5,6-*g*]quinoline (Compound **255**, structure **57** of **Scheme XVII**, where R^1=methyl, R^2=H, R^3=trifluoromethyl, Y=NH)

6-*tert*-Butyloxycarbamoyl-2-nitrotoluene (structure **65** of **Scheme XVII**, where R^1=methyl, P=*t*-butyloxycarbonl, Y=NH) This intermediate was prepared from 2-methyl-3-nitroaniline

(5.00 g, 32.8 mmol) by General Method 10 (EXAMPLE147), affording 7.44 g (90%) of 6-*tert*-butyloxycarbamoyl-2-nitrotoluene as an off-white solid. Data for 6-*tert*-butyloxycarbamoyl-2-nitrotoluene: ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.98 (br d, *J* = 8.0, 1H, 5-H), 7.51 (br d, *J* = 8.1, 1H, 3-H), 7.28 (dd, *J* = 7.6, 3.4, 1H, 4-H), 6.58 (br s, 1H, N*H*), 2.34 (s, 3H, 1-CH_3), 1.53 [s, 9H, (CH_3)$_3$CO)].

2-Amino-6-*tert*-butyloxycarbamoyltoluene (structure **66** of **Scheme XVII**, where R^1=methyl, P=*t*-butyloxycarbonl, Y=NH) This compound was prepared from 6-*tert*-butyloxycarbamoyl-2-nitrotoluene (4.60 g, 18.2 mmol) in a manner similar to that described for 3-*tert*-butyloxycarbamoylaniline (EXAMPLE 147), affording 4.00 g (99%) of 2-amino-6-*tert*-butyloxycarbamoyltoluene as a colorless oil. Data for 2-amino-6-*tert*-butyloxycarbamoyltoluene: ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.04 (br d of ABq, J_{AB} = 8.0, J_A = 0, J_B = 7.9, 2H, 5,4-H), 6.49 (d, *J* = 8.3, 1H. 3-H), 6.26 (br s, 1H, N*H*), 3.61 (br s, 2H, NH_2), 2.02 (s, 3H, 1-CH_3), 1.51 [s, 9H, (CH_3)$_3$CO)].

7-*tert*-Butyloxycarbamoyl-1,2-dihydro-2,2,4,8-tetramethylquinoline (structure **67** of **Scheme XVII**, where R^1=methyl, P=*t*-butyloxycarbonl, Y=NH) This compound was prepared from 2-amino-6-*tert*-butyloxycarbamoyltoluene (4.00 g, 18.0 mmol) according to General Method 11 (EXAMPLE 147), affording 4.56 g (84%) of 7-*tert*-butyloxycarbamoyl-1,2-dihydro-2,2,4,8-tetramethylquinoline as a white solid. Data for 7-*tert*-butyloxycarbamoyl-1,2-dihydro-2,2,4,8-tetramethylquinoline: ^{1}**H NMR** (400 MHz, $CDCl_3$) 6.94 and 6.88 (br ABq, J_{AB} = 8.3, 2H, 6,5-H), 6.16 (br s, 1H, *H*NBoc), 5.27 (s, 1H, 3-H), 3.61 (br s, 1H, (CH_3)$_2$CN*H*]) 2.04 (s, 3H, 8-CH_3), 1.97 (s, 3H, 4-CH_3), 1.50 (s, 9H, (CH_3)$_3$CO)]), 1.28 (s, 6H, 2-(CH_3)$_2$).

7-Amino-1,2-dihydro-2,2,4,8-tetramethylquinoline This compound was prepared by General Method 12 (EXAMPLE 147) from 7-*tert*-butyloxycarbamoyl-1,2-dihydro-2,2,4,8-tetramethylquinoline (400 mg, 1.32 mmol) affording 267 mg (quant) of 7-amino-1,2-dihydro-2,2,4,8-tetramethylquinoline as a light reddish oil. Data for 7-amino-1,2-dihydro-2,2,4,8-tetramethylquinoline: ^{1}**H NMR** (400 MHz, $CDCl_3$) 6.82 (d, *J* = 8.2, 1H, 5-H), 6.08 (d, *J* = 8.1, 1H, 6-H), 5.15 (d, *J* = 1.2, 1H, 3-H), 3.56 (br s, 3H, N*H*$_2$, N*H*), 1.95 (d, *J* = 1.2, 3H, 4-C*H*$_3$), 1.91 (s, 3H, 8-C*H*$_3$), 1.27 [s, 6H, 2-(C*H*$_3$)$_2$].

1,2-Dihydro-2,2,4,10-tetramethyl-6-trifluoromethyl-8-pyridono[5,6-*g*]quinoline (Compound 255, structure **57** of **Scheme XVII**, where R^1=methyl, R^2=H, R^3=trifluoromethyl, Y=NH) This compound was prepared by General Method 13 (EXAMPLE 147) from 7-amino-1,2-dihydro-2,2,4,8-tetramethylquinoline (100 mg, 0.49 mmol) and ethyl 4,4,4-trifluoroacetoacetate (107 mL, 0.73 mmol, 1.5 equivuiv) affording 75 mg (47%) of Compound **255** as a fluorescent-yellow solid. Data for Compound **255**: ^{1}**H NMR** (400 MHz, CDCl$_3$) 9.23 (br s, 1H, CON*H*), 7.37 (s, 1H, 5-H), 6.67 (s, 1H, 7-H), 5.45 (s, 1H, 3-H), 4.14 [br s, 1H, (CH$_3$)$_2$CN*H*], 2.12 (s, 3H, 10-C*H*$_3$), 2.04 (d, *J* = 1.1, 3H, 4-C*H*$_3$), 1.37 [s, 6H, 2-(C*H*$_3$)$_2$].

EXAMPLE 156

1,2-Dihydro-2,2,4-trimethyl-6-(1,1,2,2,2-pentafluoroethyl)-8-pyranono[5,6-*g*]quinoline (Compound **256**, structure **57** of **Scheme XVII**, where R^1=R^2=H, R^3=pentafluoroethyl, Y=O) This compound was prepared by General Method 9 (EXAMPLE 238) from 1,2-dihydro-7-hydroxy-2,2,4-trimethylquinoline (EXAMPLE 138) (67 mg, 0.35 mmol) and ethyl 4,4,5,5,5- pentafluoropropionylacetate (179 mg, 0.76 mmol, 2.2 equivuiv) to afford 11.8 mg (10 %) of Compound **256** as a light yellow solid. Data for Compound **256**: ^{1}**H NMR** (400 MHz, CDCl$_3$) 7.31 (s, 1 H), 6.35 (s, 1 H), 6.33 (s, 1 H), 5.40 (s, 1 H), 4.54 (s, 1 H), 1.99 (d, *J* = 1.1, 3 H), 1.35 (s, 6 H).

EXAMPLE 157

(*R/S*)-6-Chloro(difluoro)methyl-1,2,3,4-tetrahydro-2,2,4-trimethyl-8-pyranono[5,6-*g*]quinoline (Compound **257**, structure **63** of **Scheme XVIII**, where R^1=R^2=H, R^3=chlorodifluoromethyl, Y=O) This compound was prepared by General Method 9 (EXAMPLE 238) from (*R/S*)-1,2,3,4-tetrahydro-7-hydroxy-2,2,4-trimethylquinoline (EXAMPLE 150) (57 mg, 0.29 mmol) and methyl 4-chloro-4,4-difluoroacetoacetate (120 mg, 0.645 mmol, 2.2 equivuiv) to afford 35.6 mg (38 %) of Compound **257** as a light yellow solid. Data for Compound **257**: R$_f$ 0.37 (hex/EtOAc, 3:1); ^{1}**H NMR** (400 MHz, CDCl$_3$)

7.55 (s, 1 H), 6.36 (s, 1 H), 6.32 (s, 1 H), 4.53 (br s, 1 H), 2.95 (m, 1 H), 1.80 (ddd, *J* = 13, 5.1, 1.5, 1 H), 1.45 (apparent t, *J* = 13, 1 H), 1.39 (d, *J* = 6.7, 3 H), 1.32 (s, 3 H), 1.27 (s, 3 H).

EXAMPLE 158

7-Chloro-1,2-dihydro-2,2,4-trimethyl-6-trifluoromethyl-8-pyranono[5,6-*g*]quinoline (Compound **258**, structure **57** of **Scheme XVII**, where R^1=H, R^2=Cl, R^3=trifluoromethyl, Y=O) This compound was prepared by General Method 9 (EXAMPLE 238) from 1,2-dihydro-7-hydroxy-2,2,4-trimethylquinoline (EXAMPLE 138) (78 mg, 0.41 mmol) and ethyl 2-chloro-4,4,4-trifluoroacetoacetate (195 mg, 0.898 mmol, 2.2 equivuiv) to afford 7.2 mg (6%) of Compound **258** as a red solid. Data for Compound **258**: Rf 0.33 (hex/EtOAc, 3:1); **^{1}H NMR** (400 MHz, $CDCl_3$) 7.37 (s, 1 H), 6.32 (s, 1 H), 5.42 (s, 1 H), 4.54 (br s, 1 H), 2.01 (d, *J* = 1.0, 3 H), 1.31 (s, 6 H).

EXAMPLE 159

(*R/S*)-7-Chloro-1,2,3,4-tetrahydro-2,2,4-trimethyl-6-trifluoromethyl-8-pyranono[5,6-*g*]quinoline (Compound **259**, structure **63** of **Scheme XVIII**, where R^1=H, R^2=Cl, R^3=trifluoromethyl, Y=O) This compound was prepared by General Method 9 (EXAMPLE 238) from (*R/S*)-1,2,3,4-tetrahydro-7-hydroxy-2,2,4-trimethylquinoline (EXAMPLE 150) (57 mg 0.29 mmol) and ethyl 2-chloro-4,4,4-trifluoroacetoacetate (140 mg, 0.645 mmol, 2.2 equivuiv) to afford 6.8 mg (7%) of Compound **259** as a yellow solid. Data for Compound **259**: R_f 0.35 (hex/EtOAc, 3:1); **^{1}H NMR** (400 MHz, $CDCl_3$) 7.53 (s, 1 H), 6.32 (s, 1 H), 4.51 (br s, 1 H), 2.93 (m, 1 H), 1.81 (dd, *J* = 13, 3.7, 1 H), 1.44 (apparent t, *J* = 13, 3 H), 1.31 (s, 3 H), 1.25 (s, 3 H).

EXAMPLE 160

(*R/S*)-1,2,3,4-Tetrahydro-2,2,4-trimethyl-6-trifluoromethyl-8-pyridono[5,6-*g*]quinoline (Compound **260**, structure **63** of **Scheme XVIII**, where R^1=R^2=H, R^3=trifluoromethyl, Y=NH)

(*R/S*)-7-*tert*-Butyloxycarbamoyl-1,2,3,4-tetrahydro-2,2,4-trimethylquinoline (structure **72** of **Scheme XVIII**, where R^1=H, P=*t*-butyloxycarbonyl, Y=NH) To an oven-dried 100 mL round-bottomed flask containing 7-*tert*-butyloxycarbamoyl-1,2-dihydro-2,2,4-

trimethylquinoline (EXAMPLE 147) (200 mg, 0.69 mmol) in 50 mL 2:1 ethyl acetate/ethanol at rt was added 10% Pd on C (approx 1 mol%), and the mixture was stirred under an atmosphere of H_2 for 4 h. The reaction mixture was then filtered, and concentrated under diminished pressure to give 201 mg (quant) of 7-*tert*-butyloxycarbamoyl-1,2,3,4-tetrahydro-2,2,4-trimethylquinoline as a white oily solid. Data for (*R/S*)-7-*tert*-butyloxycarbamoyl-1,2,3,4-tetrahydro-2,2,4-trimethylquinoline: ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.02 (d, *J* = 8.7, 1H, 5-H), 6.73 (br s, 1H, *H*NBoc), 6.39 (dd, *J* = 8.3, 2.2, 1H, 6-H), 6.29 (br s, 1H, 8-H), 3.62 (br s, 1H, N*H*), 2.85 (ddq, *J* = 12.5, 12.3, 6.4, 1H, 4-H), 1.70 and 1.39 [d of ABq, J_{AB} = 12.8, J_A = 5.5 Hz (3-H_{equiv}), J_B = 12.6 Hz (3-H_{ax})2H], 1.49 [s, 9H, $(CH_3)_3CO)$], 1.29 (d, *J* = 6.7, 3H, 4-CH_3), 1.21 (s, 3H, 2-CH_3), 1-14 (s, 3H, 2-CH_3).

(*R/S*)-7-Amino-1,2,3,4-tetrahydro-2,2,4-trimethylquinoline This compound was prepared by General Method 12 (EXAMPLE 147) from 7-*tert*-butyloxycarbamoyl-1,2,3,4-tetrahydro-2,2,4-trimethylquinoline (150 mg, 0.51 mmol) to afford 98 mg (quant) of (*R/S*)-7-amino-1,2,3,4-tetrahydro-2,2,4-trimethylquinoline as a light reddish oil. Data for 7-amino-1,2,3,4-tetrahydro-2,2,4-trimethylquinoline: ^{1}**H NMR** (400 MHz, $CDCl_3$) 6.92 (dd, *J* = 8.0, 0.8, 1H, 5-H), 6.02 (dd, *J* = 8.2, 2.3, 1H, 6-H), 5.77 (d, *J* = 2.3, 1H, 8-H), 3.39 (br s, 3H, NH_2, N*H*), 2.81 (ddq, *J* = 12.6, 12.3, 6.4, 1H, 4-H), 1.68 and 1.38 [d of ABq, J_{AB} = 12.8, J_A = 5.5 Hz (3-H_{equiv}), J_B = 12.5 Hz (3-H_{ax})2H], 1.26 (d, *J* = 6.7, 3H, 4-CH_3), 1.19 (s, 3H, 2-CH_3), 1.14 (s, 3H, 2-CH_3).

1,2,3,4-Tetrahydro-2,2,4-trimethyl-6-trifluoromethyl-8-pyridono[5,6-*g*]quinoline (Compound **260**, structure **63** of Scheme **XVIII**, where R^1=R^2=H, R^3=trifluoromethyl, Y=NH) This compound was prepared by General Method 13 (EXAMPLE 147) from (*R/S*)-7-amino-1,2,3,4-tetrahydro-2,2,4-trimethylquinoline (98 mg, 0.51 mmol) and ethyl 4,4,4-trifluoroacetoacetate (82 mL, 0.56 mmol, 1.1 equivuiv) to afford 66 mg (42%) of Compound **260** as a fluorescent-yellow solid. Data for Compound **260**: ^{1}**H NMR** (400 MHz, $CDCl_3$) 11.32 (br s, 1H, CON*H*), 7.50 (s, 1H, 5-H), 6.64 (s, 1H, 7-H), 6.41 (s, 1H, 10-H), 4.55 [br s, 1H, $(CH_3)_2$CN*H*], 2.91 (ddq, *J* = 12.6, 12.4, 6.3, 1H, 4-H), 1.76 and 1.41

[d of ABq, J_{AB} = 12.8, J_A = 5.5 Hz (3-H_{equiv}), J_B = 12.4 Hz (3-H_{ax})2H], 1.37 (d, *J* = 6.8, 3H, 4-CH_3), 1.22 (s, 3H, 2-CH_3), 1.18 (s, 3H, 2-CH_3).

EXAMPLE 161

1,2-Dihydro-2,2,4,9-tetramethyl-6-trifluoromethyl-8-pyridono[5,6-*g*]quinoline (Compound **261**, structure **57** of Scheme XVI, where R^1=R^2=H, R^3=trifluoromethyl, R^4=methyl) To an oven-dried 50-mL r.b. flask containing Compound **247** (500.0 mg, 1.62 mmol) in 5 mL THF at 0°C was added portion-wise sodium hydride (71.4 mg of a 60% dispersion in mineral oil, 1.78 mmol, 1.10 equivuiv). After 30 min, iodomethane (101 mL, 1.62 mmol, 1.00 equivuiv) was added, and the mixture was allowed to warm to rt, and after 4 h, the reaction mixture was cooled to 0°C, and water (5 mL) was added. The reaction mixture was then diluted with 100 mL ethyl acetate, and the organic solution was washed with 50 mL brine, dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, hexanes/ethyl acetate, gradient elution) afforded 497 mg (95%) of Compound **261** as a bright fluorescent-yellow solid. Data for Compound **261**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.41 (d, *J* = 1.7, 1H, 5-H), 6.73 (s, 1H, 7-H), 6.28 (s, 1H, 10-H), 5.42 (s, 1H, 3-H), 4.36 [br s, 1H, $(CH_3)_2$CN*H*], 3.62 (s, 3H, NCH_3), 2.04 (d, *J* = 1.2, 3H, 4-CH_3), 1.33 [s, 6H, 2-(CH_3)2].

EXAMPLE 162

1,2-Dihydro-2,2,4-trimethyl-8-trifluoromethyl-6-pyridono[5,6-*g*]quinoline (Compound **262**, structure **70** of Scheme XVII, where R^1=R^2=H, R^3=trifluoromethyl, Y=NH) An alternative procedure for the Knorr reaction combined 7-amino-1,2-dihydro-2,2,4-trimethylquinoline (EXAMPLE 147) (131 mg, 0.70 mmol) and ethyl 4,4,4-trifluoroacetoacetate (154 mL, 1.05 mmol, 1.5 equivuiv) with 0.5 mL polyphosphoric acid (PPA) in a 10-mL r.b. flask and the mixture was heated to 100°C for 2 h. The cooled reaction mixture was diluted with 140 mL ethyl acetate, and the solution was washed with neutralized to pH 8 with 50 mL sat'd aqueous $NaHCO_3$. The layers were separated, and the organic phase was washed with 50 mL brine, dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, hexanes/ethyl acetate, gradient elution) afforded 79 mg (37%) of Compound **247** along with 8 mg (4%) of

Compound **262** as a fluorescent-yellow solid. Data for Compound **262**: **^{1}H NMR** (400 MHz, $CDCl_3$) 10.50 (br s, 1H, $C{=}CCF_3N\mathit{H}$), 7.33 (s, 1H, 5-H), 6.62 (s, 1H, 7-H), 6.17 (s, 1H, 10-H), 5.33 (s, 1H, 3-H), 4.21 [br s, 1H, $(CH_3)_2CN\mathit{H}$], 2.04 (s, 3H, 4-$C\mathit{H}_3$), 1.36 [s, 6H, 2-$(C\mathit{H}_3)_2$].

EXAMPLE 163

6-[Dichloro(ethoxy)methyl]-1,2-dihydro-2,2,4-trimethyl-8-pyranono[5,6-*g*]quinoline (**Compound 263, structure 57 of Scheme XVII**, where R^1=R^2=H, R^3=dichloro(ethoxy)methyl, Y=O)

This compound was prepared by General Method 9 (EXAMPLE 238) from 1,2-dihydro-7-hydroxy-2,2,4-trimethylquinoline (EXAMPLE 138) (67 mg, 0.35 mmol) and ethyl 4,4,4-trichloroacetoacetate (179 mg, 0.77 mmol, 2.2 equivuiv) to afford 30 mg (24%) of Compound **263** as a light orange solid. Data for Compound **263**: Rf 0.28 (hex/EtOAc, 3:1); **^{1}H NMR** (400 MHz, $CDCl_3$) 7.97 (s, 1 H), 6.51 (s, 1 H), 6.32 (s, 1 H), 4.42 (q, *J* = 7.2, 2 H), 2.92 (m, 1 H), 1.79 (dd, *J* = 13, 5.1, 1 H), 1.40 (m, 4 H), 1.38 (d, *J* = 6.6, 3 H), 1.30 (s, 3 H), 1.25 (s, 3 H).

EXAMPLE 164

5-(3-Furyl)-1,2-dihydro-2,2,4-trimethyl-8-pyranono[5,6-*g*]quinoline (**Compound 264, structure 57 of Scheme XVII**, where R^1=R^2=H, R^3=3-furyl, Y=O)

This compound was prepared by General Method 9 (EXAMPLE 238) from 1,2-dihydro-7-hydroxy-2,2,4-trimethylquinoline (EXAMPLE 138) (120 mg, 0.62 mmol) and ethyl ß-oxo-3-furanpropionate (227 mg, 1.25 mmol, 2 equivuiv) to afford 6.4 mg (3%) of Compound **264** as a light yellow solid. Data for Compound **264**: R_f 0.30 (hex/EtOAc, 3:1); **^{1}H NMR** (400 MHz, $CDCl_3$) 7.76 (s, 1 H), 7.76 (dd, *J* = 3.5, 1.8, 1 H), 7.34 (s, 1 H), 6. 66 (d, *J* = 1.7, 1 H), 6.35 (s, 1 H), 6.06 (s, 1 H), 5.36 (s, 1 H), 4.34 (s, 1 H), 1.95 (d, *J* = 1.1, 3 H), 1.34 (s, 6 H).

EXAMPLE 165

1,2-Dihydro-1,2,2,4-tetramethyl-6-trifluoromethyl-8-pyranono[5,6-*g*]quinoline (Compound **265, structure 60 of Scheme XVI**, where R^1=R^2=R^5=H, R^3=trifluoromethyl, Y=O)

In a dry r.b. flask equivuipped with a magnetic stir bar was dissolved Compound **238** (50 mg, 0.162 mmol) and paraformaldehyde (48 mg, 1.62 mmol, 10 equivuiv) in glacial acetic acid (10 mL). To this bright yellow solution was added $NaCNBH_3$ (50 mg, 0.81 mmol, 5 equivuiv). The solution stirred for 18 h under an atmosphere of N_2. In a separate flask was prepared a suspension of 100 g ice and 20 mL of 20% NaOH(aq). The reaction mixture was slowly poured over the NaOH solution, extracted with EtOAc (3 x 50 mL), washed with brine, dried (Na_2SO_4) and concentrated *in vacuo* to afford 50.6 mg (97%) of Compound **265** as a bright yellow solid. Data for Compound **265**: Rf 0.39 (hex/EtOAc, 3:1); ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.20 (d, J = 1.8, 1 H), 6.36 (s, 2 H), 5.36 (d, J = 1.0, 1 H), 2.88 (s, 3 H), 2.00 (d, J = 1.1, 3 H), 1.39 (s, 6 H).

EXAMPLE 166

1,2-Dihydro-6-trifluoromethyl-2,2,4-trimethyl-9-thiopyran-8-ono[5,6-*g*] quinoline (Compound **266**, structure **57** of **Scheme XVII**, where R^1=R^2=H, R^3=trifluoromethyl, Y=S)

3-Amino-*S*-*t*-butyloxycarbonyl thiophenol (structure **66** of **Scheme XVII**, where R^1=H, P=*t*-butyloxycarbonyl, Y=S) To a solution of 3-aminothiophenol (500 mg, 4.0 mmol) and di-*t*-butyl dicarbonate (872 mg, 4.0 mmol) in 10 mL of dry dichloromethane at 0°C was added dropwise, triethylamine (557 mL, 4.0 mmol). When the addition was complete, the reaction was allowed to warm to rt and the resulting mixture was stirred for 16 h. The reaction mixture was concentrated *in vacuo* and the residue was then diluted with 20 mL of ethyl acetate and washed with water (2x10 mL), dried (Na_2SO_4) and concentrated *in vacuo* to an oil that was subjected to flash chromatography (silica gel, hexanes/ethyl acetate, 7:3) which gave 274 mg (30%) of 3-amino-*S*-*t*-butyloxycarbonyl thiophenol as a clear oil. Data for 3-amino-*S*-*t*-butyloxycarbonyl thiophenol: ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.12 (apparent t, J = 8.2, 1H), 6.90 (d, J = 8.2, 1H), 6.84 (d, J = 2.2, 1H), 6.68 (dd, J = 8.2, 2.2, 1H), 3.68 (br s, 2H), 1.56 (s, 9H).

7-*t*-Butyloxycarbonylthio-1,2-dihydro-2,2,4-trimethylquinoline (structure **67** of **Scheme XVII**, where R^1=H, P=*t*-butyloxycarbonyl, Y=S) This compound was prepared by General Method 13 (EXAMPLE 147) from 3-amino-S-*t*-butyloxycarbonyl thiophenol (274 mg, 1.2

mmol) to afford 148 mg (40%) of 7-*t*-butyloxycarbonylthio-1,2-dihydro-2,2,4-trimethylquinoline as a yellowish oil. Data for 7-*t*-butyloxycarbonylthio-1,2-dihydro-2,2,4-trimethylquinoline: ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.02 (d, *J* = 7.9, 1H), 6.74 (dd, *J* = 7.9, 1.6, 1H), 6.57 (d, *J* = 1.6, 1H), 5.31 (s, 1H), 3.73 (br s, 1H), 1.95 (s, 3H), 1.50 (s, 9H), 1.26 (s, 6H).

1,2-Dihydro-6-trifluoromethyl-2,2,4-trimethyl-9-thiopyran-8-ono[5,6-*g*] quinoline (Compound **266**, structure **57** of **Scheme XVII**, where R^1=R^2=H, R^3=trifluoromethyl, Y=S) Trifluoroacetic acid (744 mL, 0.0096 mol) was added all at once *via* a syringe to a solution of 7-*t*-butyloxycarbonylthio-1,2-dihydro-2,2,4-trimethylquinoline (0.14 g) in 1 mL of dry dichloromethane at 0 °C. After 10 min the ice bath was removed and the mixture was allowed to stir at rt for 45 minutes. It was then cooled to 0 °C and neutralized with sat'd $NaHCO_3$, extracted with dichloromethane (3 x 10 mL). The combined organic phases were washed with water (10 mL), dried (Na_2SO_4) and concentrated *in vacuo* to a crude product (50 mg) that was used directly in the next step. A solution of the crude material obtained above (50 mg) and zinc chloride (100 mg, 0.724 mmol) in 0.5 mL of absolute ethanol was heated in a sealed tube for 16 h at 80 °C. The reaction was quenched with sat'd NH_4Cl (2 mL) and extracted with ethyl acetate (2 x 5 mL), dried (Na_2SO_4) and concentrated *in vacuo* to an orange solid residue that was subjected to flash chromatography (silica gel, hexanes/ethyl acetate, 7:3), followed by preparative TLC (500 µm, hexanes/ethyl acetate, 7:3) to afford 2.2 mg (3%) of Compound **266** as a yellow oil. Data for Compound **266**: ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.54 (s, 1H), 6.62 (s, 1H), 6.43 (s, 1H), 5.44 (s, 1H), 4.32 (br s, 1H), 2.03 (s, 3H), 1.29 (s, 6H).

EXAMPLE 167

1,2-Dihydro-1,2,2,4,9-pentamethyl-6-trifluoromethyl-8-pyridono[5,6-*g*]quinoline (Compound **267**, structure **60** of **Scheme XVI**, where R^1=R^2=R^5=H, R^3=trifluoromethyl, Y=N-methyl)

To a 25-mL r.b. flask containing Compound **247** (EXAMPLE 147) (125.8 mg, 0.41 mmol) in 5 mL DMF at rt was added 200 mg (approx 10 equivuiv) solid KOH. After 30 min, iodomethane (129 ML, 2.04 mmol, 5.0 equivuiv) was then added, and the mixture was allowed to stir at rt overnight. Ethyl acetate (50 mL) was then added, the biphasic mixture was neutralized to pH 6 with sat'd aqueous NH_4Cl, and the layers were separated. The organic phase was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, hexanes/ethyl acetate, gradient elution) afforded 111 mg (81%) of Compound **267** as a bright fluorescent-yellow solid. Data for Compound **267**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.37 (s, 1H, 5-H), 6.74 (s, 1H, 7-H), 6.21 (s, 1H, 10-H), 5.38 (s, 1H, 3-H), 3.69 [s, 3H, CONC*H*3], 2.94 [s, 3H, $(CH_3)_2CNCH_3$], 2.03 (s, 3H, 4-C*H*3), 1.40 [s, 6H, 2-(C*H*3)2].

EXAMPLE 168

7-Chloro-1,2-dihydro-2,2,4-trimethyl-6-trifluoromethyl-8-pyridono[5,6-g]quinoline (Compound **268**, structure **57** of Scheme **XVII**, where R^1=H, R^2=Cl, R^3=trifluoromethyl, Y=NH)

This compound was prepared by General Method 13 (EXAMPLE 147) from 7-amino-1,2-dihydro-2,2,4-trimethylquinoline (EXAMPLE 147) (64 mg, 0.34 mmol) and ethyl 2-chloro-4,4,4-trifluoroacetoacetate (147 mg, 0.68 mmol, 2.0 equivuiv) to afford 36 mg (31%) of Compound **268** as a fluorescent-yellow solid. Data for Compound **268**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.52 (s, 1H, 5-H), 6.31 (s, 1H, 10-H), 5.43 (s, 1H, 3-H), 4.47 [br s, 1H, $(CH_3)_2$CN*H*], 2.03 (s, 3H, 4-C*H*3), 1.33 [s, 6H, 2-(C*H*3)2].

EXAMPLE 169

6-Chloro(difluoro)methyl-1,2-dihydro-2,2,4-trimethyl-8-pyridono[5,6-g]quinoline (Compound **269**, structure **57** of Scheme **XVII**, where R^1=R^2=H, R^3=chloro(difluoromethyl), Y=NH)

This compound was prepared by General Method 13 (EXAMPLE 147) from 7-amino-1,2-dihydro-2,2,4-trimethylquinoline (EXAMPLE 147) (60 mg, 0.33 mmol) and methyl 4-chloro-4,4-difluoroacetoacetate (92 mg, 0.49 mmol, 1.5 equivuiv) to afford 17 mg (16%) of Compound **269** as a fluorescent-yellow solid. Data for Compound **269**: **^{1}H NMR** (400 MHz, $CDCl_3$) 12.50 (br s, 1H, CON*H*), 7.52 (s, 1H, 5-H), 6.62 (s, 1H, 7-H), 6.39 (s, 1H, 10-H), 5.42 (s, 1H, 3-H), 4.48 [br s, 1H, $(CH_3)_2$CN*H*], 2.04 (d, *J* = 1.0, 3H, 4-C*H*3), 1.31 [s, 6H, 2-(C*H*3)2].

EXAMPLE 170

8-Cyano-1,2-dihydro-2,2,4-trimethylindeno[3,2-*e*]quinoline (Compound **270**, structure **16** of **Scheme IV**, where R^{2-4}, R^6 = H, R^5=cyano, X=CH_2)

To a 25-mL r.b. flask equivuipped with a magnetic stir bar were added Compound **117** (104.7 mg, 0.40 mmol), DMF (1.5 mL), pyridine (0.16 mL), and copper (I) cyanide (43.2 mg, 0.48 mmol). A reflux condenser was attached to the flask. The green cloudy mixture was stirred at reflux for 3 hours, and allowed to cool to room temperature. The reaction mixture was diluted with ether (30 mL) which formed a precipitate in the dark solution. The precipitate was gravity filtered through Celite. The filtrate was rinsed three times with ether (20 mL). The isolated solution was added to a separatory funnel. The organic layer was washed with 2:1 mixture of water and ammonium hydroxide (20 mL) followed by saturated ammonium chloride solution (2 x 20 mL) and saturated sodium bicarbonate (20 mL). The aqueous layers were extracted with ether (3 x 10 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated. The product was purified by flash column chromatography (75 mL silica, hexane) to afford 30 mg (26 %) of Compound **270**. Data for Compound **270**: ^{1}H NMR (400 MHz, acetone-d_6) 7.77 (d, *J* = 7.9, 1H), 7.72 (s, 1 H), 7.61 (m, 2 H), 6.72 (s, 1 H), 5.54 (s, 1 H), 5.39 (s, 1 H), 3.79 (s, 2 H), 2.08 (s, 3 H), 1.29 (s, 6 H).

EXAMPLE 171

6-(3-Cyano-5-fluorophenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **271**, structure **4** of **Scheme II**, where R^1=3-cyano-5-fluorophenyl)

3-Bromo-5-fluorobenzonitrile. To a 1 liter r.b. flask equivuipped with a magnetic stir bar, commercially available 1,3-dibromo-5-fluorobenzene (44.0 g, 173.3 mmol), DMF (268 mL), pyridine (28.0 mL), and copper (I) cyanide (15.5 g, 173.3 mmol) were added under nitrogen. A reflux condenser was attached to the flask. The green cloudy mixture was stirred at reflux for 3 h. The reaction progress was difficult to monitor by TLC, so once lower Rf impurities were observed the reaction was allowed to cool to rt. The reaction mixture was quenched with 200 mL ether which formed a precipitate in the dark solution. The precipitate was gravity filtered through Celite. The filtrate was rinsed three times with ether (100 mL). The isolated solution was added to a separatory funnel. The organic layer was washed with 2 to 1 mixture of water and ammonium hydroxide (200 mL) followed by saturated ammonium chloride solution (2 x 200 mL) and saturated sodium bicarbonate (200 mL). The aqueous layers were extracted with ether (3 x 100 mL). The organic layers were combined and dried (Na_2SO_4). The product, 3-bromo-5-fluorobenzonitrile, was purified by flash column chromatography (300 mL silica, hexane) followed by recrystallization from hexane to afford 22.3 g (65 %) of the product as white crystals. Data for 3-bromo-5-fluorobenzonitrile: **^{1}H NMR** (400 MHz, acetone-d_6) 7.81 (s, 1 H), 7.73 (dd, *J* = 8.4, 1.9, 1 H), 7.65 (dd, *J* = 8.5, 2.0, 1 H).

6-(3-Cyano-5-fluorophenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **271**, structure **4** of **Scheme II**, where R^1=3-cyano-5-fluorophenyl). This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (46.3 mg, 0.14 mmol) and 3-bromo-5-fluorobenzonitrile (29.1 mg, 0.14 mmol). The crude material was purified by recrystallization from hexane to afford 15.8 mg (37%) of Compound **271**. Data for Compound **271**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.83 (app t, *J* = 1.3, 1 H), 7.68 (dd, *J* = 10.6, 4.0, 1 H), 7.43 (d, *J* = 2.0, 1 H), 7.41 (dd, *J* = 2.2, 1.2 1H) 7.35 (dd, *J* = 8.3, 2.2, 1 H), 6.59 (d, *J* = 8.4, 1 H), 5.35 (br s, 1 H), 5.39 (s, 1 H), 2.04 (s, 3 H), 1.28 (s, 6 H).

EXAMPLE 172

6-(3-Cyano-4-fluorophenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **272**, structure **4** of **Scheme II**, where R^1=3-cyano-4-fluorophenyl)

This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (53.8 mg, 0.17 mmoles) and 3-bromo-6-fluoro-benzonitrile (33.9 mg, 0.17 mmol). The crude material was purified by HPLC (reverse phase ODS column, 85% methanol/water, 3.0 mL/min) to afford 3.3 mg (7%) of Compound **272**. Data for Compound **272**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.97 (dd, *J* = 6.1, 2.2, 1 H), 7.93 (m, 1 H), 7.39 (t, *J* = 17.9, 9.0, 1 H), 7.35 (d, *J* = 1.5, 1 H), 7.27 (dd, *J* = 8.3, 1.9, 1 H), 6.58 (d, *J* = 8.3, 1 H), 5.38 (s, 1 H), 5.34 (s, 1 H), 2.08 (s, 3 H), 1.28 (s, 6 H).

EXAMPLE 173

6-(3-Cyano-6-fluorophenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **273**, structure **4** of **Scheme II**, where R^1=3-cyano-6-fluorophenyl)

This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (70.0 mg, 0.22 mmol) and 3-bromo-4-fluorobenzonitrile (44.1 mg, 0.22 mmol). The crude material was purified by HPLC (reverse phase ODS column, 85% methanol/water, 3.0 mL/min) to afford 3.3 mg (5%) of Compound **273**. Data for Compound **273**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.90 (dd, *J* = 7.5, 2.1, 1 H), 7.67 (m, 1 H), 7.36 (dd, *J* = 10.9, 8.5, 1 H), 7.28 (s, 1 H), 7.21 (m, 1 H), 6.58 (d, *J* = 8.2, 1 H), 5.48 (s, 1 H), 5.37 (s, 1 H), 2.04 (s, 3 H), 1.29 (s, 6 H).

EXAMPLE 174

6-[5-fluoro-3-(trifluoromethyl)phenyl]-1,2-dihydro-2,2,4-trimethylquinoline (Compound **274**, structure **4** of **Scheme II**, where R^1=5-fluoro-3-(trifluoromethyl)phenyl)

This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (42.8 mg, 0.13 mmol) and 3-bromo-5-fluorobenzotrifluoride (32.7 mg, 0.13 mmol). The crude material was purified by HPLC (reverse phase ODS column, 90% methanol/water, 3.0 mL/min) to afford 3.1 mg (7%) of Compound **274**. Data for Compound **274**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.71 (s, 1 H), 7.63 (d, *J* = 10.5, 1 H), 7.40 (d, *J* = 2.2, 1 H), 7.34 (dd, *J* = 8.1, 2.0, 1 H), 7.29 (d, *J* = 8.6, 1 H), 6.59 (d, *J* = 8.3, 1 H), 5.50 (s, 1 H), 5.39 (s, 1 H), 2.05 (s, 3 H), 1.29 (s, 6 H).

EXAMPLE 175

6-(3-chloro-2-methylphenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **275**, structure **4** of **Scheme II**, where R^1=3-chloro-2-methylphenyl)

This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (70.0 mg, 0.22 mmol) and 2-bromo-6-chlorotoluene (45.2 mg, 0.22 mmol). The crude material was purified by flash column chromatography (75 ml silica, hexane to 5% ethyl acetate/hexane) to afford 63.1 mg (96%) of Compound **275**. Data for Compound **275**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.30 (d, *J* = 8.3, 1 H), 7.16 (m, 1 H), 6.95 (s, 1 H), 6.87 (d, J = 10.2, 1 H), 6.54 (d, J = 8.0, 1 H), 5.36 (s, 1 H), 5.25 (s, 1 H), 2.03 (s, 3 H), 1.28 (s, 6 H).

EXAMPLE 176

1,2-Dihydro-2,2,4-trimethyl-6-(3-nitrophenyl)quinoline (Compound **276**, structure **4** of **Scheme II**, where R^1=3-nitrophenyl)

This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (19.4 mg, 0.06 mmol) and 3-nitrobromobenzene (12.3 mg, 0.06 mmol). The crude material was purified by flash column chromatography (75 ml silica, hexane to 5% ethyl acetate/hexane) followed by reverse phase flash column chromatography (50 mL ODS, 80% methanol/water) to afford 2.9 mg (16%) of Compound **276**. Data for Compound **276**: **^{1}H NMR** (400 MHz, acetone-d_6) 8.35 (app t, J = 4.1, 2.0, 1 H), 8.05 (d, J = 8.0, 1 H), 8.01 (dd, J = 8.1, 6.5, 1 H), 7.64 (t, J = 15.9, 8.0, 1 H), 7.40 (d, J = 2.1, 1 H), 7.34 (dd, J = 8.4, 2.3, 1 H), 6.61 (d, J = 8.4, 1 H), 5.40 (d, J = 1.4, 1 H), 2.05 (s, 3 H), 1.29 (s, 6 H).

EXAMPLE 177

6-(3-Acetylphenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **277**, structure **4** of **Scheme II**, where R^1=3-acetylphenyl)

This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (66.2 mg, 0.21 mmol) and 3-bromoacetophenone (41.4 mg, 0.21 mmol). The crude material was purified by flash column chromatography (30 ml silica, hexane to 20% acetone/hexane) followed by reverse phase flash column chromatography (50 mL ODS, 70% methanol/water) and a second normal phase flash column chromatography (30 mL silica, hexane to 20% acetone/hexane) to afford 5.0 mg (8%) of Compound **277**. Data for Compound **277**: **^{1}H NMR** (400 MHz, acetone-d_6) 8.13 (s, 1 H), 7.81 (m, 1 H), 7.50 (t, J = 15.0, 7.8, 1 H), 7.33 (m, 2 H), 6.59 (d, J = 8.1, 1 H), 5.38 (s, 1 H), 5.32 (s, 1 H), 2.62 (s, 3 H), 2.08 (s, 3 H), 1.28 (s, 6 H).

EXAMPLE 178

6-(3-cyano-2-methylphenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **278**, structure **4** of **Scheme II**, where R^1=3-cyano-2-methylphenyl)

3-Bromo-2-methylbenzonitrile. This compound was prepared in a manner similar to that described for 3-bromo-5-fluorobenzonitrile from commercially available 2,6-dibromotoluene (1.80 g, 7.20 mmol), DMF (11 mL), pyridine (1.1 mL), and copper (I) cyanide (0.52 g, 5.76 mmol). The crude product was purified by flash column chromatography (100 mL silica, hexane) to afford 50 mg (35 %) of 3-bromo-2-methylbenzonitrile. Data for 3-bromo-2-methylbenzonitrile: ^{1}**H NMR** (400 MHz, acetone-d_6) 7.88 (d, J = 8.0, 1 H), 7.73 (d, J = 8.0, 1 H), 7.32 (t, J = 15.8, 7.9, 1 H), 2.58 (s, 3H).

6-(3-cyano-2-methylphenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **278**, structure **4** of **Scheme II**, where R^1=3-cyano-2-methylphenyl). This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (56.5 mg, 0.18 mmol) and 3-bromo-2-methylbenzonitrile (34.8 mg, 0.18 mmol). The crude material was purified by flash column chromatography (50 ml silica, hexane to 20% acetone/hexane) followed by a second flash column chromatography (75 mL silica, hexane to 20% acetone/hexane) to afford 10.5 mg (20%) of Compound **278**. Data for Compound **278**: ^{1}**H NMR** (400 MHz, acetone-d_6) 7.59 (dd, J = 7.7, 0.9, 1 H), 7.48 (dd, J = 7.8, 0.8, 1 H), 7.36 (t, J = 15.3, 7.7, 1 H), 6.99 (d, J = 1.8, 1 H), 6.91 (dd, J = 8.1, 1.9, 1 H), 6.58 (d, J = 8.1, 1 H), 5.37 (s, 1 H), 5.30 (s, 1 H), 2.48 (s, 3 H), 1.97 (s, 3 H), 1.30 (s, 6 H).

EXAMPLE 179

1,2-Dihydro-2,2,4-trimethyl-6-(3-methylphenyl)quinoline (Compound **279**, structure **4** of **Scheme II**, where R^1=3-methylphenyl)

This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (99.5 mg, 0.31 mmol) and 3-bromotoluene (53.5 mg, 0.31mmoles). The crude material was purified by HPLC (reverse phase, ODS column, 80% methanol/water, 3.0 mL/min.) to afford 2.7 mg (3%) of Compound **279**. Data for Compound **279**: ^{1}**H NMR** (400 MHz, acetone-d_6) 7.37 (s, 1 H), 7.32 (d, J = 7.9, 1 H), 7.28 (d, J = 2.0, 1 H), 7.21 (m, 2 H), 7.02 (d, J = 7.3, 1 H), 6.55 (d, J = 8.3, 1 H), 5.36 (s, 1 H), 5.22 (s, 1 H), 2.34 (s, 3 H), 2.03 (s, 3 H), 1.27 (s, 6 H).

EXAMPLE 180

6-(5-Fluoro-3-nitrophenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **280**, structure 4 of Scheme II, where R^1=5-fluoro-3-nitrophenyl)

1-Fluoro-3-nitroiodobenzene To a 25 mL round-bottom flask equivuipped with a magnetic stir bar 3-iodo-5-nitroaniline (543.3 mg, 2.06 mmol) and methylene chloride (10 mL) were added under nitrogen. Nitrogen was bubbled through the colorless solution for 15 min. The solution was cooled to 0°C in an ice bath. At that point approximately 500 mg nitrosonium tetrafluoroborate was added in one portion making a cloudy precipitate. The reaction was allowed to continue stirring for 2 hours. The mixture was kept under nitrogen as 10 mL dry, deoxygenated ortho-dichlorobenzene was added. A distillation apparatus was fitted to the reaction flask. The flask was placed in an oil bath and was heated until the material had completely distilled over. The crude product was isolated by washing the residue through a short column (74 mL silica, hexane). Purification by silica gel chromatography (74 mL silica, hexane) afforded 279.4 mg (50 %) of 5-fluoro-3-nitroiodobenzene. Data for 5-fluoro-3-nitroiodobenzene: **^{1}H NMR** (400 MHz, acetone-d6) 8.36 (s, 1 H), 8.00 (m, 2 H).

6-(5-Fluoro-3-nitrophenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **280**, structure 4 of Scheme II, where R^1=5-fluoro-3-nitrophenyl) This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (140.2 mg, 0.44 mmol) and 5-fluoro-3-nitroiodobenzene (117.6 mg, 0.44 mmol). The crude material was purified by flash column chromatography (150 ml silica, hexane to 20% acetone/hexane) followed by a second flash column chromatography (100 mL silica, hexane to 20% acetone/hexane) to afford 95 mg (69%) of Compound **280**. Data for Compound **280**: **^{1}H NMR** (400 MHz, acetone-d_6) 8.22 (app t, *J* = 3.0, 1.5, 1 H), 7.78 (m, 1 H), 7.43 (d, *J* = 2.2, 1 H), 7.38 (dd, *J* = 8.4, 2.3, 1 H), 6.61 (d, *J* = 8.3, 1 H), 5.58 (s, 1 H), 5.40 (s, 1 H), 2.05 (s, 3 H), 1.29 (s, 6 H).

EXAMPLE 181

1,2-Dihydro-6-(3-methoxyphenyl)-2,2,4-trimethylquinoline (Compound **281**, structure 4 of Scheme II, where R^1=3-methoxyphenyl)

This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (79.1 mg, 0.25 mmol) and 3-bromoanisole (46.5 mg, 0.25 mmol). The crude material was purified by flash column chromatography (75 mL silica, hexane to 10 %ethyl acetate/hexane) to afford 2.1 mg (3 %) of Compound **281**. Data for Compound **281**: ^{1}H NMR (400 MHz, acetone-d_6) 7.25 (m, 2 H), 7.11 (d, *J* = 6.9, 1 H), 7.07 (app t, *J* = 4.1, 2.2, 1 H), 6.78 (dd, *J* = 8.6, 2.2, 1 H), 6.55 (d, *J* = 8.3, 1 H), 5.36 (s, 1 H), 5.26 (s, 1 H), 3.82 (s, 3 H), 2.03 (s, 3 H), 1.27 (s, 6 H).

EXAMPLE 182

6-(5-Cyano-3-pyridyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **282**, structure **4** of Scheme II, where R^1=5-cyano-3-pyridyl)

This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (45.6 mg, 0.14 mmol) and 3-cyano-5-bromopyridine (26.2 mg, 0.14 mmol). The crude material was purified by flash column chromatography (100 mL silica, hexane) to afford 10.4 mg (26%) of Compound **282**. Data for Compound **282**: ^{1}H NMR (400 MHz, acetone-d_6) 8.21 (d, *J* = 1.7, 1 H), 7.79 (m, 2 H), 7.44 (d, *J* = 2.1, 1 H), 7.39 (dd, *J* = 8.4, 2.3, 1 H), 6.61 (d, *J* = 8.2, 1 H), 5.59 (s, 1 H), 5.40 (s, 1 H), 2.05 (s, 3 H), 1.29 (s, 6 H).

EXAMPLE 183

1,2-Dihydro-2,2,4-trimethyl-6-(2-methyl-3-nitrophenyl)quinoline (Compound **283**, structure **4** of Scheme II, where R^1=2-methyl-3-nitrophenyl)

This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (170.6 mg, 0.54 mmol) and 2-bromo-6-nitrotoluene (115.8 mg, 0.54 mmol). The crude material was purified by flash column chromatography (80 ml silica, hexane to 20% acetone/hexane) followed by a second flash column chromatography (75 mL silica, hexane to 20% acetone/hexane) to afford 68 mg (41%) of Compound **283**. Data for Compound **283**: ^{1}H NMR (400 MHz, acetone-d_6) 7.71 (d, *J* = 7.9, 1 H), 7.49 (dd, *J* = 7.4, 0.9, 1 H), 7.41 (t, *J* = 15.6, 7.9, 1 H), 6.99 (d, *J* = 1.8, 1 H), 6.91 (dd, *J* = 8.1, 1.9, 1 H), 6.57 (d, *J* = 8.2, 1 H), 5.37 (s, 1 H), 5.32 (s, 1 H), 2.35 (s, 3 H), 1.97 (s, 3 H), 1.29 (s, 6 H).

EXAMPLE 184

6-(2-Amino-3,5-difluorophenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **284**, structure **4** of **Scheme II**, where R^1=2-amino-3,5-difluorophenyl)

This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (48.8 mg, 0.15 mmol) and 2-bromo-4,6-difluoroaniline (31.9 mg, 0.15 mmol). The crude material was purified by flash column chromatography (ODS reverse phase, 80% methanol/water) to afford 15 mg (33%) of Compound **284**. Data for Compound **284**: **^{1}H NMR** (400 MHz, acetone-d$_6$) 7.10 (d, *J* = 2.0, 1 H), 7.02 (dd, *J* = 8.1, 2.0, 1 H), 6.80 (m, 1 H), 6.69 (m, 1 H) 6.56 (d, *J* = 8.1, 1 H), 5.36 (s, 1 H), 5.34 (s, 1 H), 4.22 (br s, 2 H), 1.97 (s, 3 H), 1.28 (s, 6 H).

EXAMPLE 185

6-(3-Bromo-2-chloro-5-fluorophenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **285**, structure **4** of **Scheme II**, where R^1=3-bromo-2-chloro-5-fluorophenyl)

This compound was prepared according to General Method 2 (EXAMPLE 9) from Compound **9** (143.3 mg, 0.45 mmol) and 1-chloro-2,6-dibromo-4-fluorobenzene (129.9 mg, 0.45 mmol). The crude material was purified by flash column chromatography (50 mL silica, hexane) followed by reverse phase preparatory TLC (1000 mL ODS, 80% methanol/water) to afford 4.3 mg (3%) of Compound **285**. Data for Compound **285**: **^{1}H NMR** (400 MHz, acetone-d$_6$) 7.50 (dd, *J* = 7.8, 3.0, 1 H), 7.19 (dd, *J* = 9.2, 3.0, 1 H), 7.10 (d, *J* = 2.0, 1 H), 7.03 (dd, *J* = 8.1, 2.0, 1 H), 6.55 (d, *J* = 8.3, 1 H), 5.61 (s, 1 H), 5.37 (s, 1 H), 1.97 (s, 3 H), 1.29 (s, 6 H).

EXAMPLE 186

6-(3-Cyano-5-fluorophenyl)-1,2-dihydro-2,2,4-trimethyl-3-quinolone (Compound **286**, structure **79** of **Scheme XX**, where R^1=R^3=R^5=H, R^2=cyano, R^4=fluoro, P=*t*-butoxycarbonyl)

In a 100 mL r.b. flask, a solution of 1,2-dihydro-6-(3-cyano-5-fluorophenyl)-2,2,4-trimethyl-1-*t*-butoxycarbonylquinoline (structure 77 of **Scheme XX**, where R^1=R^3=R^5=H, R^2=cyano, R^4=fluoro, P=*t*-butoxycarbonyl, an intermediate from EXAMPLE 171) (134.8 mg, 0.34 mmol) in THF (17.2 mL) was treated with a 1.0 M THF solution of BH_3-THF (1.29 mL, 1.3

mmol, 3.9 equivuiv). The reaction mixture was stirred for 20 min, then poured into a cold (0°C) 10 M solution of NaOH (50 mL), ether (50 mL), and 30% hydrogen peroxide (10 mL). The reaction mixture was stirred overnight (16 h). The reaction mixture was extracted with ether (3 x 20 mL). The extracts were combined, dried (Na_2SO_4), and concentrated. The crude material was dissolved in CH_2Cl_2 (2 mL) and treated with PCC (50 mg). The reaction mixture was stirred for 1 h, filtered through a pad of Celite, and concentrated. Purification by flash column chromatography (175 mL silica, hexane) afforded 1.3 mg (1%) of Compound **286** as a white solid. Data for Compound **286**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.90 (s, 1 H), 7.75 (d, *J* = 10.6, 1 H), 7.54 (m, 2 H), 7.48 (d, *J* = 8.3, 1 H), 6.95 (d, *J* = 8.2, 1 H), 5.52 (s, 1 H), 3.61 (m, 1 H), 1.49 (d, *J* = 7.05, 3 H), 1.33 (s, 3 H), 1.23 (s, 3 H).

EXAMPLE 187

6-(3-Fluoro-2-methylphenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **287**, structure **4** of **Scheme II**, where R^1=3-fluoro-2-methylphenyl)

This compound was prepared by General Method 2 (EXAMPLE 9) from Compound **9** (50 mg, 0.158 mmol) and 2-bromo-6-fluorotoluene (60 mg, 0.315 mmol). Purification by flash chromatography on silica gel (20g) using 5% EtOAc:hexanes afforded 6 mg (14%) of Compound **287** as a yellow oil. Data for Compound **287**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.20 (m, 1H), 7.02 (m, 1H), 6.98 (m, 2H), 6.91 (m, 1H), 6.56 (d, *J*=8.0, 1H), 5.37 (s, 1H), 5.29 (br s, 1H), 2.19 (s, 3H), 1.98 (s, 3H), 1.28 (s, 6H).

EXAMPLE 188

1,2-Dihydro-2,2,4-trimethyl-6-(3-methylthiophenyl)quinoline (Compound **288**, structure **4** of **Scheme II**, where R^1=3-methylthiophenyl)

This compound was prepared by General Method 2 (EXAMPLE 9) from Compound **9** (50 mg, 0.158 mmol) and 3-bromothioanisole (64 mg, 0.315 mmol). Purification by flash chromatography on silica gel (20 g) using 5% EtOAc:hexanes afforded 7 mg (15%) of Compound **288** as a yellow oil. Data for Compound **288**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.43 (s, 1H), 7.32 (m, 3H), 7.24 (m, 2H), 7.14 (m, 1H), 6.57 (d, *J*=8.1, 1H), 5.37 (s, 1H), 5.31 (br s, 1H), 2.53 (s, 3H), 1.28 (s, 6H).

EXAMPLE 189

6-(5-Chloro-2-thienyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **289**, structure **4** of **Scheme II**, where R^1=5-chloro-2-thienyl)

This compound was prepared by General Method 2 (EXAMPLE 9) from Compound **9** (50 mg, 0.158 mmol) and 2-bromo-5-chlorothiophene (63 mg, 0.315 mmol). Purification by flash chromatography on silica gel (20 g) using 5% EtOAc:hexanes afforded 10 mg (22%) of Compound **289** as a yellow oil. Data for Compound **289**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.21 (d, *J* = 2.1, 1H), 7.1 (dd, *J* = 8.1, 2.0, 1H), 7.02 (d, *J* = 3.7, 1H), 6.93 (d, *J* = 3.7, 1H), 6.51 (d, 8.3, 1H), 5.42 (br s, 1H), 5.40 (s, 1H), 2.01 (s, 3H), 1.27 (s, 6H).

EXAMPLE 190

1,2-Dihydro-2,2,4-trimethyl-6-(3-methyl-2-thienyl)quinoline (Compound **290**, structure **4** of **Scheme II**, where R^1=3-methyl-2-thienyl)

This compound was prepared by General Method 2 (EXAMPLE 9) from Compound **9** (50 mg, 0.158 mmol) and 2-bromo-3-methylthiophene (57 mg, 0.315 mmol). Purification by flash chromatography on silica gel (20 g) using 5% EtOAc:hexanes afforded 5 mg (12%) of Compound **290** as a yellow oil. Data for Compound **290**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.18 (d, *J* = 5.2, 1H), 7.09 (d, *J* = 1.9, 1H), 7.03 (dd, *J* = 8.1, 2.0, 1H), 6.88 (d, 5.1, 1H), 6.54 (d, *J* = 8.1, 1H), 5.38 (s, 1H), 5.32 (br s, 1H), 2.26 (s, 3H), 1.99 (s, 3H), 1.29 (s, 6H).

EXAMPLE 191

8-Fluoro-1,2-dihydro-2,2,4-trimethyl-6-(3-nitrophenyl)quinoline (Compound **291**, structure 83 of **Scheme XXI**, where R^1=R^{3-7}=R^9=H, R^8=F)

4-Amino-3-fluoro-3'-nitrobiphenyl (structure 82 of **Scheme XXI**, where R^1=R^{3-7}=H, R^8=F)

General Method 14: Suzuki Coupling of a 4-Bromoaniline with an Arylboronic Acid. A mixture of 3-nitrobenzeneboronic acid (0.70 g, 4.2 mmol), 4-bromo-2-fluoroaniline (730 mg, 4.0 mmol), $(PPh_3)_4Pd$ (93 mg, 0.08 mmol), and K_2CO_3 (0.69 g, 5.0 mmol) in toluene (20 mL) and water (2 mL) was heated at 95 °C for 16 h and the mixture was diluted with EtOAc (20 mL). The mixture was washed with water (10 mL) and brine (10 mL), concentrated and purified by silica gel chromatography to afford the 4-amino-3-fluoro-3'-nitrobiphenyl (structure 82 of **Scheme XXI**, where R^1=R^{3-7}=H, R^8=F) (0.4 g, 41%) as a yellow solid.

8-Fluoro-1,2-dihydro-2,2,4-trimethyl-6-(3-nitrophenyl)quinoline (Compound **291**, structure 83 of **Scheme XXI**, where R^1=R^{3-7}=R^9=H, R^8=F). This compound was prepared by General Method 8 (EXAMPLE 138) from 4-amino-3-fluoro-3'-nitrobiphenyl (0.4 g, 1.7 mmol) to afford 101 mg (19%) of Compound **291** as a red solid, in addition to 0.8 g of the starting aminobiphenyl. Data for Compound **291**: **IR** (neat) 3400, 2968, 1531, 1506, 1346; **^{1}H NMR** (400 MHz, $CDCl_3$) 8.35 (t, *J* = 2.0, 1 H), 8.10 (dd, *J* = 7.8, 2.0, 1 H), 7.80 (d, *J* = 7.8, 1 H), 7.54 (t, *J* = 7.8, 1 H), 7.14 (d, *J* = 11.7, 1 H), 7.11 (d, *J* = 1.8, 1 H), 5.43 (s, 1 H), 4.07 (bs, 1 H), 2.07 (s, 3 H), 1.35 (s, 6 H); **^{13}C NMR** (100 MHz, $CDCl_3$) 150.4 (d, *J* = 237), 149.0, 142.6, 132.2, 132.1, 130.0, 129.8, 128.0, 126.2 (d, *J* = 7.0), 124.0, 121.2, 121.1, 117.8, 113.0 (d, *J* = 20), 52.1, 31.7, 19.1.

EXAMPLE 192

1,2-Dihydro-6-(3-nitrophenyl)-2,2,4,8-tetramethylquinoline (Compound **292**, structure 86 of **Scheme XXII**, where R^1=R^{3-5}=H, R^2=nitro)

4-Bromo-2-methylaniline (5.58 g, 30 mmol) was treated with iodine (0.2 g, 0.9 mmol) and acetone (150 mL) in a sealed tube at 80 °C for 24 h to provide 6-bromo-1,2-dihydro-8-methylquinoline (Compound **85** of **Scheme XXII**) in 9 % yield as a yellow oil (0.70g). Most of the aniline (>80%) was recovered. A mixture of the 6-bromo-1,2-dihydro-8-methylquinoline (90 mg, 0.33 mmol), 3-nitrobenzeneboronic acid (167 mg, 1.0 mmol), $Pd(PPh_3)_4$ (24 mg, 0.02 mmol), K_2CO_3 (190 mg, 1.38 mmol) in toluene (7 mL) and water (1.5 mL) was heated at 70 °C for 16 h. Standard work-up followed by chromatography afforded 23 mg (23%) of Compound **292** as a yellow oil. Data for Compound **292**: **IR** (neat) 3412, 2966, 1602, 1530, 1348; **^{1}H NMR** (400 MHz, $CDCl_3$) 8.38 (t, *J* = 2.0, 1 H), 8.08 (dd, *J* = 7.8 and 2.0, 1 H), 7.85 (d, *J* = 7.8, 1 H), 7.52 (t, *J* = 7.8, 1 H), 7.24 (d, *J* = 11.7, 1 H), 7.21 (d, *J* = 1.9, 1 H), 5.39 (s, 1 H), 3.72 (bs, 1 H), 2.18 (s, 3 H), 2.07 (s, 3 H), 1.34 (s, 6 H); **^{13}C NMR** (100 MHz, $CDCl_3$) 148.9, 143.7, 142.0, 132.2, 129.6, 128.8, 128.7, 128.6, 126.5, 121.3, 121.0, 120.7, 120.6, 120.3, 52.3, 31.9, 19.2, 17.3.

EXAMPLE 193

6-(5-Bromo-3-pyridyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **293**, structure **4** of **Scheme II**, where R^1=5-bromo-3-pyridyl)

This compound was prepared by General Method 2 (EXAMPLE 9) from 3,5-dibromopyridine (119 mg, 0.5 mmol) and Compound **9** (50 mg, 0.16 mmol) to afford 18 mg (35%) of Compound **290** as a yellow oil. Data for Compound **290**: **^{1}H NMR** (400 MHz, $CDCl_3$) 8.69 (s, 1 H), 8.52 (s, 1 H), 7.93 (t, *J* = 2.0, 1 H), 7.21 (d, *J* = 2.1, 1 H), 7.20 (dd, *J* = 8.1, 2.1, 1 H), 6.50 (d, *J* = 8.1, 1 H), 5.37 (s, 1 H), 3.88 (bs, 1 H), 2.05 (s, 3 H), 1.31 (s, 6 H).

EXAMPLE 194

6-(3-Bromo-2-pyridyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **294**, structure **4** of **Scheme II**, where R^1=3-bromo-2-pyridyl)

This compound was prepared by General Method 2 (EXAMPLE 9) from 2,6-dibromopyridine (237 mg, 1.0 mmol) and Compound **9** (100 mg, 0.32 mmol) to afford 42 mg (40%) of Compound **294** as a yellow oil. Data for Compound **294**: **IR** (neat) 3379, 2966, 1604, 1575, 1433, 1124; **^{1}H NMR** (400 MHz, $CDCl_3$) 7.68 (d, *J* = 1.9, 1 H), 7.66 (dd, *J* = 8.1, 1.9, 1 H), 7.54 (d, *J* = 7.8, 1 H), 7.49 (t, *J* = 7.8, 1 H), 7.23 (d, *J* = 7.8, 1 H), 6.49 (d, *J* = 8.1, 1 H), 5.35 (s, 1 H), 3.93 (bs, 1 H), 2.08 (s, 3 H), 1.30 (s, 6 H); **^{13}C NMR** (100 MHz, $CDCl_3$) 159.3, 145.1, 142.1, 138.8, 128.7, 128.6, 127.7, 126.6, 124.6, 122.6, 121.5, 117.6, 113.1, 52.4, 31.6, 18.9.

EXAMPLE 195

6-(3-Bromo-2-thienyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **295**, structure **4** of **Scheme II**, where R^1=3-bromo-2-thienyl)

This compound was prepared by General Method 2 from 2,5-dibromothiophene (242 mg, 1.0 mmol) and Compound **9** (50 mg, 0.16 mmol) to afford 24 mg (45%) of Compound **295** as a yellow oil. Data for Compound **295**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.17 (bs, 1 H), 7.15 (dd, *J* = 8.1, 1.9, 1 H), 6.95 (d, *J* = 3.7, 1 H), 6.86 (bs, 1 H), 6.42 (bs, 1 H), 5.36 (s, 1 H), 3.80 (bs, 1 H), 2.01 (s, 3 H), 1.29 (s, 6 H).

EXAMPLE 196

1,2-Dihydro-6-(2,3,5,6-tetrafluoro-4-pyridyl)-2,2,4-trimethylquinoline (Compound **296**, structure **4** of **Scheme II**, where R^1=2,3,5,6-tetrafluoro-4-pyridyl)

This compound was prepared by General Method 2 from 4-bromo-2,3,5,6-tetrafluoropyridine (150 mg, 0.63 mmol) and Compound **9** (50 mg, 0.16 mmol) to afford 13.4 mg (26%) of Compound **296** as a white solid. Data for Compound **296**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.23 (s, 1 H), 7.20 (d, *J* = 7.9, 1 H), 6.51 (d, *J* = 7.9, 1 H), 5.38 (s, 1 H), 4.08 (bs, 1 H), 2.00 (s, 3 H), 1.33 (s, 6 H); **^{13}C NMR** (100 MHz, $CDCl_3$) 145.4, 144.5 (dd, *J* = 230, 16), 139.3 (dd, *J* = 256, 33), 130.7 (d, *J* = 17.2), 129.0, 128.6, 125.7, 123.8, 121.1, 113.8, 113.1, 112.6, 52.7, 32.1, 18.7.

EXAMPLE 197

5,8-Difluoro-1,2-dihydro-6-(3-nitrophenyl)-2,2,4-trimethylquinoline (Compound **297**, structure **83** of **Scheme XXI**, where R^1=R^{3-5}=R^7=R^9=H, R^2=nitro, R^6=R^8=fluoro) This compound was prepared by the same procedure as described in the synthesis of Compound **291** (EXAMPLE 191) from 4-bromo-2,5-difluoroaniline (32 mg, 0.13 mmol) and 3-nitrobenzeneboronic acid (167 mg, 1.0 mmol) to afford 3 mg (10%) of Compound **297** as a colorless oil. Data for Compound **297**: **^{1}H NMR** (400 MHz, $CDCl_3$) 8.33 (t, *J* = 1.6, 1 H), 8.14 (dd, *J* = 8.0, 1.6, 1 H), 7.78 (d, *J* = 8.0, 1 H), 7.57 (t, *J* = 8.0, 1 H), 6.94 (dd, *J* = 10.8, 6.3, 1 H), 5.37 (s, 1 H), 4.16 (bs, 1 H), 2.17 (dd, *J* = 7.0, 1.3, 3 H), 1.34 (s, 6 H).

EXAMPLE 198

2,4-Diethyl-8-fluoro-1,2-dihydro-2-methyl-6-(3-nitrophenyl)quinoline (Compound **298**, structure **83** of **Scheme XXI**, where R^1=R^{3-7}=H, R^2=nitro, R^8=fluoro, R^9=methyl) A mixture of 2-fluoro-4-(3-nitrophenyl)aniline (100 mg, 0.43 mmol), iodine (10 mg, 0.039 mmol) and 2-butanone (5 mL) was heated at 100 °C in a sealed tube for 16 h. Removal of solvent and chromatography of the crude mixture on a silica gel column afforded 4 mg (3%) of Compound **298** as a yellow oil. Data for Compound **298**: **^{1}H NMR** (400 MHz, $CDCl_3$) 8.33 (t, *J* = 2.0, 1 H), 8.10 (dd, *J* = 7.8, 2.0, 1 H), 7.81 (d, *J* = 7.8, 1 H), 7.54 (t, *J* = 7.8, 1

H), 7.14 (s, 1 H), 7.12 (d, J = 11.0, 1 H), 5.30 (s, 1 H), 3.96 (bs, 1 H), 2.47 (q, J = 7.5, 2 H), 1.57 (q, J = 7.5, 2 H), 1.31 (s, 3 H), 1.21 (t, J = 7.5, 3 H), 0.95 (t, J = 7.5, 3 H).

EXAMPLE 199

6-(3-Bromophenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **299**, structure **4** of Scheme **II**, where R^1= 3-bromophenyl)

This compound was prepared by General Method 2 (EXAMPLE 9) from Compound **9** (100 mg, 0.32 mmol) and 1,3-dibromobenzene (0.20 mL, 1.60 mmol). The crude product was purified by prep TLC (5 x 20 cm, 250mm, 25% EtOAc:hexane) to afford 2.3 mg (2%) of Compound **299** as a white solid. Data for compound **299**: Rf=0.43 (silica gel, 25% EtOAc:hexane); ^{1}**H NMR** (400 MHz, acetone-d_6) 7.72(s, 1 H), 7.56 (d, J = 8.5, 1 H), 7.38(d, J = 8.5, 1 H), 7.37 (m, 2 H), 7.24 (d, J = 8.5, 1 H), 6.58 (d, J = 8.5, 1 H), 5.39 (br m, 2 H), 2.04 (s, 3 H), 1.29 (s, 6 H).

EXAMPLE 200

1,2-Dihydro-2,2,4-trimethyl-6-(5-nitro-2-thienyl)quinoline (Compound **300**, structure **4** of Scheme **II**, where R^1= 5-nitro-2-thienyl)

This compound was prepared by General Method 2 (EXAMPLE 9) from Compound **9** (50 mg, 0.16 mmol) and 2-bromo-5-nitrothiophene (0.16 g, 0.79 mmol). The crude product was purified by prep TLC (20 x 20cm, 1000mm, 25% EtOAc:hexane) to afford 50 mg (81%) of Compound **300** as a purple solid. Data for compound **300**: Rf=0.40 (silica gel, 25% EtOAc:hex); ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.85 (d, J = 4.3, 1 H), 7.27 (m, 2 H), 7.04 (d, J = 4.3, 1 H), 6.43 (d, J = 8.5, 1 H), 5.38 (brs, 1 H), 4.13 (brs, 1 H), 2.03 (s, 3 H), 1.32 (s, 6 H).

EXAMPLE 201

1,2-Dihydro-6-(2,4,5-trifluorophenyl)-2,2,4-trimethylquinoline (Compound **301**, structure **4** of Scheme **II**, where R^1= 2,4,5-trifluorophenyl)

This compound was prepared by General Method 2 (EXAMPLE 9) from compound **9** (50 mg, 0.16 mmol) and 2,4,5-trifluorobromobenzene (0.10 mL, 0.79 mmol). The crude product was purified by prep TLC (5 x 20cm, 250mm, 25% EtOAc:hexane) to afford 15 mg

(31%) of Compound **301** as a yellow oil. Data for compound **301**: Rf=0.40 (silica gel, 25% EtOAc:hex); ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.21 (m, 1 H), 7.18 (s, 1 H), 7.13 (d, J = 8.5, 1 H), 6.96 (m, 1 H), 6.47 (d, J = 8.5, 1 H), 5.34 (s, 1 H), 3.83 (brs, 1 H), 2.01 (s, 3 H), 1.31 (s, 6 H).

EXAMPLE 202

6-(3-Bromo-5-fluorophenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **302**, structure **4** of Scheme **II**, where R^1= 3-bromo-5-fluorophenyl)

This compound was prepared by General Method 2 (EXAMPLE 9) from compound **9** (50 mg, 0.16 mmol) and 1,3-dibromo-5-fluorobenzene (0.20 mL, 1.60 mmol). The crude product was purified by prep TLC (20 x 20cm, 500mm, 25% EtOAc:hexane) to afford 20 mg (36%) of Compound **302** as a colorless oil. Data for compound **302**: Rf=0.40 (silica gel, 25% EtOAc:hex); ^{1}**H NMR**(400 MHz, $CDCl_3$) 7.44 (s, 1 H), 7.21 to 7.09 (m, 4 H), 6.46 (d, J = 8.5, 1 H), 5.35 (s, 1 H), 3.80 (brs, 1H), 2.04 (s, 3 H), 1.30 (s, 6 H).

EXAMPLE 203

6-(5-Carboxaldehyde-3-thienyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **303**, structure **4** of Scheme **II**, where R^1= 3-thienyl-5-carboxaldehyde)

This compound was prepared by General Method 2 (EXAMPLE 9) from compound **9** (50 mg, 0.16 mmol) and 4-bromo-2-thiophenecarboxaldehyde (0.15 g, 0.79 mmol). The crude product was purified by prep TLC (20 x 20cm, 1000mm, 25% EtOAc:hexane) to afford 31 mg (70%) of Compound **303** as a yellow oil. Data for compound **303**: Rf=0.44 (silica gel, 25% EtOAc:hex); ^{1}**H NMR**(400 MHz, $CDCl_3$) 9.95 (s, 1 H), 7.96 (s, 1 H), 7.66 (s, 1 H), 7.25 (s, 1 H), 7.22 (d, J = 3.8, 1 H), 6.47 (d, J = 8.5, 1 H), 5.37 (s, 1 H), 3.84 (brs, 1 H), 2.04 (s, 3 H), 1.31 (s, 6 H).

EXAMPLE 204

1,2-Dihydro-2,2,4,7-tetramethyl-6-(3-nitrophenyl)quinoline (Compound **304**, structure **83** of **Scheme XXI**, where R^1=R^{3-5}=R^6=R^{8-9}=H, R^2=nitro, R^7=methyl)

4-Amino-2-methyl-3'-nitrobiphenyl (structure 82 of **Scheme XXI**, where R^1=R^{3-5}=R^6=R^8=H, R^2=nitro, R^7=methyl). This compound was made according to the General

Method 14 (EXAMPLE 191) from 3-nitrobenzene-boronic acid (673.2 mg, 3.82 mmol) and 4-bromo-3-methylaniline (710.2 mg, 3.82 mmol) to afford 540 mg (62%) of 4-amino-2-methyl-3'-nitrobiphenyl (structure 82 of **Scheme XXI**, where R^1=R^{3-5}=R^6=R^8=H, R^2=nitro, R^7=methyl). Data for 4-amino-2-methyl-3'-nitrobiphenyl: **^{1}H NMR** (400 MHz, acetone-d_6) 8.13 (dd, *J* = 7.5, 1.1, 1H), 8.09 (dd, *J* = 3.9, 1.8, 1H), 7.73 (ddd, *J* = 7.7, 1.6, 1.4, 1H), 7.66 (dd, *J* = 8.0, 7.8, 1H), 6.99 (d, *J* = 8.0, 1H), 6.60 (m, 1H), 4.73 (br s, 1H), 2.18 (s, 3H).

1,2-Dihydro-2,2,4,7-tetramethyl-6-(3-nitrophenyl)quinoline (Compound **304**, structure **83** of **Scheme XXI**, where R^1=R^{3-5}=R^6=R^{8-9}=H, R^2=nitro, R^7=methyl). This compound was prepared according to General Method 8 (EXAMPLE 138) from 540 mg of 4-amino-2-methyl-3'-nitrobiphenyl. Approximately 10% of the reaction mixture was worked up and purified to afford 1.5 mg of Compound **304**. Data for Compound **304**: **^{1}H NMR** (400 MHz, acetone-d_6) 8.13 (m, 2 H), 7.76 (dd, *J* = 8.9, 1.2, 1 H), 7.69 (t, *J* = 15.9, 8.0, 1 H), 6.93 (s, 1 H), 6.43 (s, 1 H), 5.32 (s, 1 H), 2.14 (s, 3 H), 1.95 (s, 3 H), 1.27 (s, 6 H).

EXAMPLE 205

6-(5-Fluoro-2-methoxy-3-nitrophenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **305**, structure **4** of Scheme **II**, where R^1= 5-fluoro-2-methoxy-3-nitrophenyl) This compound was prepared by General Method 2 (EXAMPLE 9) from compound **9** (60 mg, 0.19 mmol) and 2-bromo-4-fluoro-6-nitroanisole (37 mg, 0.15 mmol). The crude product was purified by silica gel chromatography (EtOAc/hexane, 10:1) to afford 5 mg (8%) of Compound **305** as a yellow oil. Data for compound **305**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.34 (dd, *J* = 7.3, 3.3, 1H), 7.25 (m, 3H), 7.21 (dd, *J* = 8.1, 2.0, 1H), 6.50 (d, *J* = 8.3, 1H), 5.37 (s, 1H), 3.89 (s, 1H), 3.55 (s, 3H), 2.01 (d, *J* = 1.4, 1H), 1.33 (s, 6H).

EXAMPLE 206

6-(3-Chloro-2-methoxyphenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **306**, structure **4** of Scheme **II**, where R^1= 3-chloro-2-methoxyphenyl) This compound was prepared by General Method 2 (EXAMPLE 9) from compound **9** (60 mg, 0.19 mmol) and 2-bromo-6-chloroanisole (33 mg, 0.15 mmol). The crude product was purified by silica gel chromatography (EtOAc/hexane, 10:1) to afford 6 mg (8%) of Compound **306** as a yellow oil. Data for compound **306**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.30 (m, 2H), 7.20 (m, 2H), 7.05 (t, *J* = 8.0, 1H), 6.51 (d, *J* = 8.3, 1H), 5.34 (s, 1H), 3.75 (s, 1H), 3.52 (s, 3H), 2.01 (s, 3H), 1.34 (s, 6H).

EXAMPLE 207

1,2-Dihydro-2,2,4-trimethyl-6-(2,3,4-trifluorophenyl)quinoline (Compound **307**, structure **4** of Scheme **II**, where R^1= 2,3,4-trifluorophenyl)

This compound was prepared by General Method 2 (EXAMPLE 9) from compound **9** (60 mg, 0.19 mmol) and 1-bromo-2,3,4-trifluorobenzene (0.11 mL, 0.93 mmol). The crude product was purified by silica gel chromatography (EtOAc/hexane, 10:1) to afford 30 mg (53%) of Compound **307** as white crystals. Data for compound **307**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.28 (m, 1H), 7.20 (m, 2H), 7.13 (dt, *J* = 8.2, 1.9, 1H), 6.58 (d, *J* = 8.3, 1H), 5.43 (br s, 1H), 5.39 (s, 1H), 2.00 (d, *J* = 1.3, 3H), 1.30 (s, 6H).

EXAMPLE 208

6-(3-Bromo-2-methylphenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound **308**, structure **4** of Scheme **II**, where R^1= 3-bromo-2-methylphenyl)

This compound was prepared by General Method 2 (EXAMPLE 9) from compound **9** (50 mg, 0.16 mmol) and 2,6-dibromotoluene (0.16 g, 0.64 mmol). The crude product was purified by silica gel chromatography (EtOAc/hexane, 10:1) to afford 27 mg (50%) of Compound **308** as a colorless glass. Data for compound **308**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.49 (d, *J* = 8.3, 1H), 7.17 (d, *J* = 6.9, 1H), 7.04 (t, *J* = 7.7, 1H), 6.95 (d, *J* = 1.9, 1H), 6.89 (dd, *J* = 8.0, 1.9, 1H), 6.46 (d, *J* = 8.0, 1H), 5.35 (s, 1H), 3.77 (br s, 1H), 1.97 (d, *J* = 1.2, 3H), 1.32 (s, 6H).

EXAMPLE 209

7-Chloro-1,2-dihydro-2,2,4-trimethyl-6-(3-nitrophenyl)quinoline (Compound **309**, structure **83** of **Scheme XXI**, where R^1=R^{3-5}=R^6=R^{8-9}=H, R^2=nitro, R^7=chloro)

2-Chloro-4-amino-3'-nitrobiphenyl (structure 82 of **Scheme XXI**, where R^1=R^{3-5}=R^{7-8}=H, R^2=nitro, R^6=chloro). This compound was prepared by General Method 14 (EXAMPLE

191) from 3-nitrobenzeneboronic acid (0.25 g, 1.5 mmol), 4-bromo-3-chloroaniline (0.21 g, 1.0 mmol), and $(PPh_3)_4Pd$ (35 mg, 0.030 mmol) to afford 0.08 g (32%) of 2-chloro-4-amino-3'-nitrobiphenyl as an orange solid. Data for 2-chloro-4-amino-3'-nitrobiphenyl: **^{1}H NMR** (400 MHz, acetone-d_6) 8.29 (app t, *J* = 2.0, 1H), 8.18 (dt, *J* = 9.0, 1.2, 1H), 7.76 (dd, *J* = 9.0, 1.2, 1H), 7.56 (t, *J* = 8.0, 1H), 7.14 (d, *J* = 8.2, 1H), 6.82 (d, *J* = 2.2, 1H), 6.65 (dd, *J* = 8.2, 2.2, 1H), 3.86 (br s, 2H).

7-Chloro-1,2-dihydro-2,2,4-trimethyl-6-(3-nitrophenyl)quinoline (Compound **309**, structure **83** of Scheme XXI, where R^1=R^{3-6}=R^{8-9}=H, R^2=nitro, R^7=chloro). This compound was prepared by General Method 8 (EXAMPLE 138) from 2-chloro-4-amino-3'-nitrobiphenyl (0.08 g, 0.3 mmol) to afford 15 mg (15%) of Compound **309** as an orange solid, in addition to 2 mg (2%) of Compound **310** (EXAMPLE 210) as an orange solid. The structures of Compounds **309** and **310** were secured by n.O.e. experiments. Data for Compound **309**: **^{1}H NMR** (400 MHz, acetone-d_6) 8.77 (t, *J* = 2.0, 1H), 8.21 (dt, *J* = 9.0, 1.2, 1H), 7.88 (dd, *J* = 6.6, 1.6, 1H), 7.71 (t, *J* = 7.9, 1H), 7.10 (s, 1H), 6.67 (s, 1H), 5.43 (s, 1H), 1.99 (s, 3H), 1.32 (s, 6H).

EXAMPLE 210

5-Chloro-1,2-dihydro-2,2,4-trimethyl-6-(3-nitrophenyl)quinoline (Compound **310**, structure **83** of Scheme XXI, where R^1=R^{3-5}=R^{7-9}=H, R^2=nitro, R^6=chloro)

This compound (2 mg, 2%) was obtained along with Compound **309** (EXAMPLE 209) as described above. Data for Compound **310**: **^{1}H NMR** (400 MHz, acetone-d_6) 8.21 (d, *J* = 1.4, 1H), 8.20 (m, 1H), 7.81 (dt, *J* = 8.8, 1.4, 1H), 7.70 (m, 1H), 7.01 (d, *J* = 8.1, 1H), 6.71 (d, *J* = 8.1, 1H), 5.74 (br s, 1H), 5.55 (d, *J* = 1.3, 1H), 2.31 (d, *J* = 1.3, 3H), 1.28 (s, 6H).

EXAMPLE 211

8-Chloro-1,2-dihydro-2,2,4-trimethyl-6-(3-nitrophenyl)quinoline (Compound **311**, structure **83** of Scheme XXI, where R^1=R^{3-7}=R^9=H, R^2=nitro, R^8=chloro)

3-Chloro-4-amino-3'-nitrobiphenyl (structure **82** of Scheme XXI, where R^1=R^{3-7}=H, R^2=nitro, R^8=chloro). This compound was prepared by General Method 14 (EXAMPLE 191) from 3-nitrobenzeneboronic acid (0.25 g, 1.5 mmol), 4-bromo-2-chloroaniline (0.21 g, 1.0 mmol), and $(PPh_3)_4Pd$ (35 mg, 0.030 mmol) to afford a crude material which was used directly in the next step.

8-Chloro-1,2-dihydro-2,2,4-trimethyl-6-(3-nitrophenyl)quinoline (Compound **311**, structure 83 of **Scheme XXI**, where $R^1=R^{3-7}=R^9=H$, R^2=nitro, R^8=chloro). This compound was prepared by General Method 8 (EXAMPLE 138) from the crude biphenyl amine obtained above to afford 2 mg (1%) of Compound **311** as an orange solid. Data for Compound **311**: ^{1}**H NMR** (400 MHz, acetone-d_6) 8.48 (d, J = 2.0, 1H), 8.11 (dd, J = 8.0, 2.0, 1H), 8.04 (dd, J = 6.6, 1.6, 1H), 7.67 (t, J = 8.0, 1H), 7.55 (d, J = 2.0, 1H), 7.40 (d, J = 2.0, 1H), 5.43 (s, 1H), 1.99 (s, 3H), 1.29 (s, 6H).

EXAMPLE 212

8-Ethyl-1,2-dihydro-2,2,4-trimethyl-6-(3-nitrophenyl)quinoline (Compound **312**, structure 83 of **Scheme XXI**, where $R^1=R^{3-7}=R^9=H$, R^2=nitro, R^8=ethyl)

4-Amino-3-ethyl-3'-nitrobiphenyl (structure 82 of **Scheme XXI**, where $R^1=R^{3-7}=H$, R^2=nitro, R^8=ethyl). This compound was prepared by General Method 14 (EXAMPLE 191) from 3-nitrobenzeneboronic acid (0.47 g, 2.8 mmol), 4-bromo-2-ethylaniline (432 mg, 2.16 mmol), and $(PPh_3)_4Pd$ (75 mg, 0.065 mmol) to afford 139 mg (20%) of 4-amino-3-ethyl-3'-nitrobiphenyl. Data for 4-amino-3-ethyl-3'-nitrobiphenyl: ^{1}**H NMR** (400 MHz, acetone-d_6) 8.38 (t, J = 2.1, 1H), 8.08 (m, 1H), 8.00 (m, 1H), 7.66 (t, J = 8.0, 1H), 7.45 (d, J = 2.3, 1H), 7.39 (dd, J = 8.3, 2.3, 1H), 6.83 (d, J = 8.3, 1H), 4.68 (br s, 2H).

8-Chloro-1,2-dihydro-2,2,4-trimethyl-6-(3-nitrophenyl)quinoline (Compound **311**, structure 83 of **Scheme XXI**, where $R^1=R^{3-7}=R^9=H$, R^2=nitro, R^8=chloro). This compound was prepared by General Method 8 (EXAMPLE 138) from the crude biphenyl amine obtained above to afford 2 mg (1%) of Compound **311** as an orange solid. Data for Compound **311**: ^{1}**H NMR** (400 MHz, acetone-d_6) 8.38 (t, J = 2.1, 1H), 8.06 (m, 2H), 7.66 (t, J = 8.0, 1H), 7.34 (m, 1H), 5.44 (s, 1H), 4.88 (br s, 1H), 2.60 (q, J = 7.5, 2H), 2.08 (s, 3H), 1.34 (s, 6H), 1.23 (t, J = 7.5, 3H).

EXAMPLE 213

9-Chloro-1,2-dihydro-2,2-dimethyl-5-coumarino[3,4-*f*]quinoline (Compound **313**, structure **88** of **Scheme XXIII**, where R^{1-2}=R^{4-6}=R^9=H, R^7=R^8=methyl, R^3=chloro)

2-Amino-6-chloro-3,4-benzocoumarin (structure 87 of **Scheme XXIII**, where R^{1-2}=R^{4-6}=H, R^3=chloro, an intermediate from EXAMPLE 109) (100 mg, 0.407 mmol) and 1,1-dimethyl propargyl acetate (52 mg, 0.41 mmol) were dissolved in THF (5 mL) and treated with triethylamine (57 µL, 0.41 mmol). The resulting solution was treated with CuCl (20 mg, 0.20 mmol). The reaction mixture was heated at relux for 16 h. The reaction was quenched with 1% (v/v) HCl (2 mL) and diluted with EtOAc (20 mL). The mixture was poured into a separatory funnel and the aqueous layer was extracted with EtOAc (2 x 20 mL). The combined organics were washed with brine (1 x 20 mL), dried (Na_2SO_4), filtered, and concentrated onto Celite. The material was purified by flash chromatography on silica gel (50 g) using 15% EtOAc:hexanes as eluent to afford 50 mg of the dimethyl propargyl amine intermediate. This material was dissolved in THF and treated with CuCl (2 mg, 0.02 mmol) and heated at reflux for 16 h. The reaction was quenched with 1 % (v/v) HCl (2 mL) and diluted with EtOAc and water. The reaction mixture was poured into a separatory funnel and the aqueous was extracted with EtOAc (2 x 20 mL). The combined organics were washed with brine (15 mL), dried (Na_2SO_4), filtered, and concentrated onto Celite. The material was purified by flash chromatography on silica gel (20 g) using 15% EtOAc:hexanes to afford 30 mg (24%) of Compound **313** as a yellow solid. Data for Compound **313**: **^{1}H NMR** (400 MHz, acetone-d_6) 8.07 (d, J = 2.4, 1H), 7.99 (d, J = 8.7, 1H), 7.91 (d, J = 10.4, 1H), 7.38 (dd, J = 8.6, 2.4, 1H), 7.26 (d, J = 8.7, 1H), 7.10 (d, J = 8.5, 1H), 6.04 (br s,1H), 5.74 (dd, J = 10.4, 1.4, 1H), 1.36 (s, 6H).

EXAMPLE 214

1,2-Dihydro-9-methoxy-2,2,4-trimethyl-5-coumarino[3,4-*f*]quinoline (Compound 314, structure **41** of **Scheme XI**, where R^1=H, R^2=methoxy)

2,5-Dimethoxyphenylboronic acid (structure **37** of **Scheme XI**, where R^1=H, R^2=methoxy). This compound was prepared in a manner similar to that of 5-fluoro-2-methoxyphenylboronic acid (EXAMPLE 107) from 1-bromo-2,5-dimethoxybenzene (2.00 mL, 13.3 mmol), *n*-BuLi (2.5 M in hexanes; 5.34 mL, 13.3 mmol), and trimethylborate (4.5

mL, 40 mmol) to afford 2.43 g (99%) of 2,5-dimethoxyphenylboronic acid which was used without further purification.

Methyl (2',5'-dimethoxy-4-nitro-2-biphenylcarboxylate). This compound was prepared in a manner similar to that of methyl 5'-fluoro-2'-methoxy-4-nitro-2-biphenylcarboxylate (EXAMPLE 107) from methyl 2-bromo-5-nitrobenzoate (2.46 g, 9.46 mmol), $(PPh_3)_4Pd$ (0.33 g, 0.28 mmol), and 2,5-dimethoxyphenylboronic acid (2.42 g, 13.3 mmol) to afford 2.08 g (69%) of methyl (2',5'-dimethoxy-4-nitro-2-biphenylcarboxylate) as a white solid. Data for methyl (2',5'-dimethoxy-4-nitro-2-biphenylcarboxylate): **^{1}H NMR** (400 MHz, $CDCl_3$) 8.70 (d, J = 2.4, 1H), 8.37 (dd, J = 8.4, 2.5, 1H), 7.52 (d, J = 8.5, 1H), 6.92 (dd, J = 8.8, 3.0, 1H), 6.84 (m, 1H), 3.82 (s, 3H), 3.75 (s, 3H), 3.67 (s, 3H).

2',5'-Dimethoxy-4-nitro-2-biphenylcarboxylic acid. This compound was prepared in a manner similar to that of 5'-fluoro-2'-methoxy-4-nitro-2-biphenylcarboxylic acid (EXAMPLE 107) from methyl 2',5'-dimethoxy-4-nitro-2-biphenylcarboxylate (2.07 g) to afford 1.93 g (99%) of 2',5'-dimethoxy-4-nitro-2-biphenylcarboxylic acid as a white solid. Data for 2',5'-dimethoxy-4-nitro-2-biphenylcarboxylic acid: **^{1}H NMR** (400 MHz, acetone-d_6) 8.64 (d, J = 2.5, 1H), 8.43 (dd, J = 8.4, 2.6, 1H), 7.67 (d, J = 8.5, 1H), 6.94 (m, 2H), 3.80 (s, 3H), 3.68 (s, 3H).

6-Methoxy-2-nitro-3,4-benzocoumarin. This compound was prepared in a manner similar to that of 6-fluoro-2-nitro-3,4-benzocoumarin (EXAMPLE 107) from 2',5'-dimethoxy-4-nitro-2-biphenylcarboxylic acid (1.93 g, 6.36 mmol), $SOCl_2$ (0.47 mL, 6.4 mmol), and $AlCl_3$ (0.67 g, 5.0 mmol) to afford 1.71 g (99%) of 6-methoxy-2-nitro-3,4-benzocoumarin as an orange powder. Data for 6-methoxy-2-nitro-3,4-benzocoumarin: **^{1}H NMR** (400 MHz, acetone-d_6) 9.04 (d, J = 2.4, 1H), 8.74 (d, J = 8.9, 1H), 8.69 (dd, J = 8.9, 2.4, 1H), 7.92 (d, J = 2.9, 1H), 7.41 (d, J = 9.0, 1H), 7.30 (dd, J = 9.0, 2.9, 1H), 3.97 (s, 3H).

2-Amino-6-methoxy-3,4-benzocoumarin (structure **40** of **Scheme XI**, where R^1=H, R^2=methoxy). This compound was prepared in a manner similar to that of 2-amino-6-fluoro-3,4-benzocoumarin (EXAMPLE 107) from 6-methoxy-2-nitro-3,4-benzocoumarin

(1.71 g, 6.3 mmol) to afford 1.27 g (80%) of 2-amino-6-methoxy-3,4-benzocoumarin as a white solid. Data for 2-amino-6-methoxy-3,4-benzocoumarin: **^{1}H NMR** (400 MHz, acetone-d_6) 8.10 (d, *J* = 8.7, 1H), 7.60 (d, *J* = 2.8, 1H), 7.55 (d, *J* = 2.5, 1H), 7.25 (m, 2H), 6.99 (dd, *J* = 8.7, 2.8, 1H), 3.90 (s, 3H).

1,2-Dihydro-9-methoxy-2,2,4-trimethyl-5-coumarino[3,4-*f*]quinoline (Compound **314**, structure **41** of Scheme **XI**, where R^1=H, R^2=methoxy). This compound was prepared in a manner similar to that of Compound 207 from 2-amino-6-methoxy-3,4-benzocoumarin (1.27 g, 5.0 mmol) to afford 0.25 g (15%) of Compound **314** as a yellow solid. Data for Compound **314**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.73 (d, *J* = 8.6, 1H), 7.35 (d, *J* = 2.8, 1H), 7.23 (d, *J* = 8.9, 1H), 7.00 (d, *J* = 8.6, 1H), 6.92 (dd, *J* = 8.9, 2.8, 1H), 5.57 (s, 1H), 4.29 (br s, 1H), 3.88 (s, 3H), 2.11 (d, *J* = 1.1, 3H), 1.33 (s, 6H).

EXAMPLE 215

9-Fluoro-1,2-dihydro-2,2,4,11-tetramethyl-5-coumarino[3,4-*f*]quinoline (Compound **315**, structure **88** of Scheme **XXIV**, where R^{1-2}=R^4=R^6=H, R^3=fluoro, R^5=R^{7-9}=methyl)

Methyl 2'-fluoro-5'-methoxy-6-methyl-4-nitro-2-biphenylcarboxylate (structure **92** of Scheme **XXIV**, where R^{1-2}=R^4=R^6=H, R^3=fluoro, R^5=methyl). This compound was prepared in a manner similar to that of methyl 5'-fluoro-2'-methoxy-4-nitro-2-biphenylcarboxylate (EXAMPLE 107) from methyl 2-bromo-3-methyl-5-nitrobenzoate (1.73 g, 6.31 mmol), $(PPh_3)_4Pd$ (0.22 g, 0.19 mmol), and 5-fluoro-2-methoxyphenylboronic acid (EXAMPLE 107) (1.50 g, 8.8 mmol) to afford 0.77 g (38%) of methyl 2'-fluoro-5'-methoxy-6-methyl-4-nitro-2-biphenylcarboxylate. Data for 2'-fluoro-5'-methoxy-6-methyl-4-nitro-2-biphenylcarboxylate: 8.61 (d, *J* = 2.3, 1H), 8.27 (d, *J* = 2.4, 1H), 7.09 (m, 1H), 6.91 (dd, *J* = 9.0, 4.3, 1H), 6.73 (dd, *J* = 8.2, 3.0, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 2.19 (s, 3H).

2'-Fluoro-5'-methoxy-4-nitro-2-biphenylcarboxylic acid. This compound was prepared in a manner similar to that of 5'-fluoro-2'-methoxy-4-nitro-2-biphenylcarboxylic acid (EXAMPLE 107) from methyl 2'-fluoro-5'-methoxy-6-methyl-4-nitro-2-biphenylcarboxylate

(0.77 g) to afford 0.73 g (99%) of 2'-fluoro-5'-methoxy-4-nitro-2-biphenylcarboxylic acid as a white solid, which was used in the next step without further purfication.

6-Fluoro-4-methyl-2-nitro-3,4-benzocoumarin. This compound was prepared in a manner similar to that of 6-fluoro-2-nitro-3,4-benzocoumarin (EXAMPLE 107) from 2'-fluoro-5'-methoxy-4-nitro-2-biphenylcarboxylic acid (0.73 g, 2.4 mmol), $SOCl_2$ (0.18 mL, 2.4 mmol), and $AlCl_3$ (0.32 g, 2.4 mmol) to afford 0.63 g (95%) of 6-fluoro-4-methyl-2-nitro-3,4-benzocoumarin as an orange powder. Data for 6-fluoro-4-methyl-2-nitro-3,4-benzocoumarin: ^{1}**H NMR** (400 MHz, acetone-d_6) 8.99 (d, *J* = 2.5, 1H), 8.63 (d, *J* = 2.5, 1H), 8.29 (dd, *J* = 10.9, 2.4, 1H), 7.53 (m, 2H), 3.14 (s, 3H).

2-Amino-6-fluoro-4-methyl-3,4-benzocoumarin (structure **87** of **Scheme XXIV**, where $R^{1-2}=R^4=R^6=H$, R^3=fluoro, R^5=methyl). This compound was prepared in a manner similar to that of 2-amino-6-fluoro-3,4-benzocoumarin (EXAMPLE 107) from 6-fluoro-4-methyl-2-nitro-3,4-benzocoumarin (0.61 g) to afford 0.54 g (99%) of 2-amino-6-fluoro-4-methyl-3,4-benzocoumarin as a white solid, which was used in the next step without further purification.

9-Fluoro-1,2-dihydro-2,2,4,11-tetramethyl-5-coumarino[3,4-*f*]quinoline (Compound **315**, structure **88** of **Scheme XXIV**, where $R^{1-2}=R^4=R^6=H$, R^3=fluoro, $R^5=R^{7-9}$=methyl). This compound was prepared in a manner similar to that of Compound **207** from 2-amino-6-fluoro-4-methyl-3,4-benzocoumarin (0.54 g) to afford 0.29 g (40%) of Compound **315** as a yellow solid. Data for Compound **315**: ^{1}**H NMR** (400 MHz, acetone-d_6) 7.87 (dd, *J* = 11.4, 2.9, 1H), 7.32 (dd, *J* = 9.0, 5.1, 1H), 7.28 (m, 1H), 7.02 (s, 1H), 5.52 (d, *J* = 1.2, 1H), 2.76 (s, 3H), 2.01 (s, 3H), 1.30 (s, 6H).

EXAMPLE 216

1,2-Dihydro-2,2,4,9-tetramethyl-5-coumarino[3,4-*f*]quinoline (Compound **316**, structure **41** of **Scheme XI**, where R^1=H, R^2=methyl)

2-Methoxy-5-methylphenylboronic acid (structure **37** of **Scheme XI**, where R^1=H, R^2=methyl). This compound was prepared in a manner similar to that of 5-fluoro-2-methoxyphenylboronic acid (EXAMPLE 107) from 2-bromo-4-methylanisole (2.00 g, 9.94

mmol), *n*-BuLi (2.5 M in hexanes; 4.00 mL, 10 mmol), and trimethylborate (3.4 mL, 30 mmol) to afford 1.60 g (96%) of 2-methoxy-5-methylphenylboronic acid which was used without further purification.

Methyl 2'-methoxy-5'-methyl-4-nitro-2-biphenylcarboxylate. This compound was prepared in a manner similar to that of methyl 5'-fluoro-2'-methoxy-4-nitro-2-biphenylcarboxylate (EXAMPLE 107) from methyl 2-bromo-5-nitrobenzoate (1.80 g, 6.92 mmol), $(PPh_3)_4Pd$ (0.33 g, 0.28 mmol), and 2-methoxy-5-methylphenylboronic acid (1.58 g, 9.51 mmol) to afford 2.03 g (98%) of methyl 2'-methoxy-5'-methyl-4-nitro-2-biphenylcarboxylate as a white solid. Data for methyl (2'-methoxy-5'-methyl-4-nitro-2-biphenylcarboxylate) : **^{1}H NMR** (400 MHz, $CDCl_3$) 8.69 (d, *J* = 2.5, 1H), 8.36 (dd, *J* = 8.4, 2.5, 1H), 7.51 (d, *J* = 8.5, 1H), 7.20 (m, 1H), 7.07 (d, *J* = 2.1, 1H), 6.81 (d, *J* = 8.4, 1H), 3.75 (s, 3H), 3.69 (s, 3H), 2.35 (s, 3H).

2'-Methoxy-5'-methyl-4-nitro-2-biphenylcarboxylic acid. This compound was prepared in a manner similar to that of 5'-fluoro-2'-methoxy-4-nitro-2-biphenylcarboxylic acid (EXAMPLE 107) from methyl 2'-methoxy-5'-methyl-4-nitro-2-biphenylcarboxylate (2.02 g) to afford 1.93 g (99%) of 2'-methoxy-5'-methyl-4-nitro-2-biphenylcarboxylic acid as a white solid. Data for 2'-methoxy-5'-methyl-4-nitro-2-biphenylcarboxylic acid: **^{1}H NMR** (400 MHz, acetone-d_6) 8.63 (d, *J* = 2.5, 1H), 8.42 (dd, *J* = 8.5, 2.5, 1H), 7.63 (d, *J* = 8.5, 1H), 7.19 (m, 1H), 7.14 (d, *J* = 2.2, 1H), 6.93 (d, *J* = 8.4, 1H), 3.70 (s, 3H), 2.32 (s, 3H).

6-Methyl-2-nitro-3,4-benzocoumarin. This compound was prepared in a manner similar to that of 6-fluoro-2-nitro-3,4-benzocoumarin (EXAMPLE 107) from 2'-methoxy-5'-methyl-4-nitro-2-biphenylcarboxylic acid (1.92 g, 6.68 mmol), $SOCl_2$ (0.49 mL, 6.7 mmol), and $AlCl_3$ (0.89 g, 6.7 mmol) to afford 1.65 g (97%) of 6-methyl-2-nitro-3,4-benzocoumarin as an orange powder. Data for 6-methyl-2-nitro-3,4-benzocoumarin: **^{1}H NMR** (400 MHz, acetone-d_6) 9.04 (d, *J* = 2.5, 1H), 8.69 (m, 2H), 8.26 (s, 1H), 7.53 (d, *J* = 8.6, 1H), 7.35 (d, *J* = 8.6, 1H), 2.49 (s, 3H).

2-Amino-6-methyl-3,4-benzocoumarin (structure **40** of **Scheme XI**, where R^1=H, R^2=methyl). This compound was prepared in a manner similar to that of 2-amino-6-fluoro-3,4-benzocoumarin (EXAMPLE 107) from 6-methyl-2-nitro-3,4-benzocoumarin (1.64 g) to afford 1.40 g (99%) of 2-amino-6-methyl-3,4-benzocoumarin as a white solid, which was used in the next step without further purification.

1,2-Dihydro-2,2,4,9-tetramethyl-5-coumarino[3,4-*f*]quinoline (Compound **316**, structure **41** of **Scheme XI**, where R^1=H, R^2=methyl). This compound was prepared in a manner similar to that of Compound **207** from 2-amino-6-methyl-3,4-benzocoumarin (1.40 g) to afford 0.738 g (38%) of Compound **316** as a yellow solid. Data for Compound **316**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.96 (d, *J* = 8.6, 1H), 7.89 (s, 1H), 7.19 (d, *J* = 8.6, 1H), 7.18 (m, 1H), 7.14 (d, *J* = 8.4, 1H), 6.04 (br s, 1H), 5.51 (s, 1H), 2.41 (s, 3H), 1.29 (s, 6H). The C(4) methyl is obscured by the acetone multiplet.

EXAMPLE 217

7-Chloro-1,2-dihydro-2,2,4-trimethyl-5-coumarino[3,4-*f*]quinoline (Compound **317**, structure **88** of **Scheme XXIV**, where R^1=chloro, R^{2-6}=H, R^{7-9}=methyl)

3-Chloro-2-methoxyphenylboronic acid (structure **90** of **Scheme XXIV**, where R^1=chloro, R^{2-4}=H). This compound was prepared in a manner similar to that of 5-fluoro-2-methoxyphenylboronic acid (EXAMPLE 107) from 2-bromo-6-chloroanisole (0.71 g, 3.2 mmol), *n*-BuLi (2.5 M in hexanes; 1.28 mL, 3.2 mmol), and trimethylborate (1.09 mL, 9.6 mmol) to afford 0.55 g (91%) of 3-chloro-2-methoxyphenylboronic acid which was used without further purification.

Methyl (3'-chloro-2'-methoxy-4-nitro-2-biphenylcarboxylate). This compound was prepared in a manner similar to that of methyl (5'-fluoro-2'-methoxy-4-nitro-2-biphenylcarboxylate) (EXAMPLE 107) from methyl 2-bromo-5-nitrobenzoate (0.58 g, 2.2 mmol), $(PPh_3)_4Pd$ (77 mg, 0.066 mmol), and 5-chloro-2-methoxyphenylboronic acid (0.54 g, 2.9 mmol) to afford 245 mg (35%) of methyl (3'-chloro-2'-methoxy-4-nitro-2-biphenylcarboxylate) as a clear oil. Data for methyl (3'-chloro-2'-methoxy-4-nitro-2-biphenylcarboxylate): **^{1}H NMR** (400 MHz, $CDCl_3$) 8.79 (d, *J* = 2.4, 1H), 8.40 (dd, *J* = 8.4, 2.4, 1H), 7.57 (d, *J* = 8.5, 1H), 7.45 (m, 1H), 7.15 (m, 2H), 3.75 (s, 3H), 3.47 (s, 3H).

3'-Chloro-2'-methoxy-4-nitro-2-biphenylcarboxylic acid. This compound was prepared in a manner similar to that of 5'-fluoro-2'-methoxy-4-nitro-2-biphenylcarboxylic acid (EXAMPLE 107) from methyl (3'-chloro-2'-methoxy-4-nitro-2-biphenylcarboxylate) (230mg) to afford 0.21 g (99%) of 3'-chloro-2'-methoxy-4-nitro-2-biphenylcarboxylic acid as a white solid. Data for 3'-chloro-2'-methoxy-4-nitro-2-biphenylcarboxylic acid: **^{1}H NMR** (400 MHz, acetone-d_6) 8.76 (d, *J* = 2.5, 1H), 8.50 (dd, *J* = 8.4, 2.5, 1H), 7.74 (d, *J* = 8.5, 1H), 7.51 (dd, *J* = 7.9, 1.8, 1H), 7.31 (dd, *J* = 7.4, 1.8, 1H), 7.24 (t, *J* = 7.9), 3.47 (s, 3H).

8-Chloro-2-nitro-3,4-benzocoumarin. This compound was prepared in a manner similar to that of 6-fluoro-2-nitro-3,4-benzocoumarin (EXAMPLE 107) from 3'-chloro-2'-methoxy-4-nitro-2-biphenylcarboxylic acid (0.20 g, 0.65 mmol), $SOCl_2$ (50 mL, 0.69 mmol), and $AlCl_3$ (85 mg, 0.65 mmol) to afford 0.18 g (99%) of 8-chloro-2-nitro-3,4-benzocoumarin as yellow crystals. Data for 8-chloro-2-nitro-3,4-benzocoumarin: **^{1}H NMR** (400 MHz, acetone-d_6) 9.06 (t, *J* = 1.4, 1H), 8.74 (s, 2H), 8.45 (dd, *J* = 8.0, 1.4, 1H), 7.32 (dd, *J* = 8.0, 1.2, 1H), 7.51 (t, *J* = 8.0, 1H).

2-Amino-8-chloro-3,4-benzocoumarin (structure **87** of Scheme **XXIV**, where R^1=chloro, R^{2-6}=H). This compound was prepared in a manner similar to that of 2-amino-6-fluoro-3,4-benzocoumarin (EXAMPLE 107) from 8-chloro-2-nitro-3,4-benzocoumarin (0.18 g, 0.65 mmol) to afford 0.10 g (62%) of 2-amino-8-chloro-3,4-benzocoumarin as a white solid, which was used in the next step without further purification.

7-Chloro-1,2-dihydro-2,2,4-trimethyl-5-coumarino[3,4-*f*]quinoline (Compound **317**, structure **88** of Scheme **XXIV**, where R^1=chloro, R^{2-6}=H, R^{7-9}=methyl). This compound was prepared in a manner similar to that of Compound **207** from 2-amino-9-chloro-3,4-benzocoumarin (0.10 g) to afford 24 mg (18%) of Compound **317** as a yellow solid. Data for Compound **317**: **^{1}H NMR** (400 MHz, acetone-d_6) 8.04 (dd, *J* = 8.1, 1.1, 1H), 7.98 (d, *J* = 8.7, 1H), 7.48 (dd, *J* = 9.0, 1.1, 1H), 7.28 (t, *J* = 8.8, 1H), 7.23 (d, *J* = 8.6, 1H), 6.24 (br s, 1H), 5.55 (d, *J* = 1.2, 1H), 2.08 (s, 3H), 1.31 (s, 6H).

EXAMPLE 218

5-(3-Fluorobenzyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **318**, structure **32** of **Scheme IX**, where R = 3-fluorobenzyl)

To a solution of Compound **225** (EXAMPLE 125) (10 mg, 0.03 mmol) in CH_2Cl_2 (5 ml) was added triethylsilane (0.05 ml, 0.3 mmol) and trifluoroacetic acid (0.024 ml, 0.3 mmol) at rt. The reaction was monitored by TLC and was found to be complete after 15 hours. The reaction mixture was quenched with an aqueous 10% NaOH solution (5mL) then extracted with EtOAc (10 mL). The organic layer was washed with brine (3 x 5 mL), dried (Na_2SO_4), then concentrated *in vacuo* to afford a yellow oil. The crude product was purified by prep TLC (5 x 20cm, 250mm, 1:1 CH_2Cl_2:hexane) to afford 1.0 mg (8%) of Compound **318** as a yellow oil. Data for Compound **318**: Rf=0.26 (silica gel, 25% EtOAc:hex); **^{1}H NMR** (400 MHz, $CDCl_3$) 7.66 (d, *J* = 8.5, 1 H), 7.48(d, *J*= 8.5 1 H), 7.23 (m, 2 H), 7.03 (m, 1 H), 6.89 (m, 3 H), 6.61 (d, *J*= 8.5, 1 H), 6.10 (m, 1 H), 5.49 (s, 1 H), 3.98 (brs, 1 H), 3.10 (m, 1 H), 2.73 (m, 1 H), 2.29 (s, 3 H), 1.29 (s, 3 H), 1.19 (s, 3 H).

EXAMPLE 219

(*R/S*)-9-Chloro-1,2-dihydro-5-methoxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **319**, structure **47** of **Scheme XIV**, where R^1=H, R^2=chloro, R^3=methyl, X=O)

(*R/S*)-9-chloro-1,2-dihydro-5-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (structure **46** of **Scheme XIV**, where R^1=H, R^2=chloro) and 6-(5-chloro-2-hydroxyphenyl)-1,2-dihydro-5-hydroxymethyl-2,2,4-trimethylquinoline (structure 94 of **Scheme XXV**, where R^{1-2}=R^{4-6}=H, R^3=chloro, R^{7-9} =methyl). Compound **209** (EXAMPLE 109) (100 mg, 0.307 mmol) was dissolved in THF, cooled to -40°C, and treated with DIBAL (614 µL, 0.614 mmol, 1 M in THF, Aldrich), warming to -20°C over 30 min. The reaction mixture was quenched with NH_4Cl (sat) (2 mL) and allowed to warm to rt. The reaction mixture was poured into a separatory funnel containing EtOAc and water. The aqueous was extracted with EtOAc (2 x 20 mL). The combined organics were washed with NaCl (sat) (1 x 15 mL), dried (Na_2SO_4), filtered, and concentrated onto Celite. The material was purified by flash chromatography using 25% EtOAc:hexanes to afford 65 mg of (*R/S*)-9-chloro-1,2-dihydro-5-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (structure **46** of

Scheme XIV, where R^1=H, R^2=chloro) and 20 mg of 6-(5-chloro-2-hydroxyphenyl)-1,2-dihydro-5-hydroxymethyl-2,2,4-trimethylquinoline (structure 94 of **Scheme XXV**, where R^{1-2}=R^{4-6}=H, R^3=chloro, R^{7-9} =methyl). Data for (*R/S*)-9-chloro-1,2-dihydro-5-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline: **^{1}H NMR** (400 MHz, acetone-d_6) 7.71 (d, *J* = 2.4, 1H), 7.55 (d, *J* = 8.4, 1H), 7.11 (dd, *J* = 8.5, 2.4, 1H), 6.94 (d, *J* = 8.4, 1H), 6.84 (d, *J* = 5.9, 1H), 6.78 (d, *J* = 8.2, 1H), 6.01 (d, *J* = 6.0, 1H), 5.56 (bs, 1H), 5.52 (s, 1H), 2.36 (s, 3H), 1.31 (s, 3H), 1.18 (s, 3H). Data for 6-(5-chloro-2-hydroxyphenyl)-1,2-dihydro-5-hydroxymethyl-2,2,4-trimethylquinoline: **^{1}H NMR** (400 MHz, acetone-d_6) 7.18 (dd, *J* = 8.5, 3.0, 1H), 7.10 (d, *J* = 2.5, 1H), 6.92 (d, *J* = 8.6, 1H), 6.75 (d, *J* = 8.0, 1H), 6.63 (d, *J* = 8.1, 1H), 5.46 (s, 1H), 5.25 (s, 1H), 4.55 (ABq, *J* = 11.4, 2H), 2.35 (s, 3H), 1.27 (s, 6H).

(*R/S*)-9-Chloro-1,2-dihydro-5-methoxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **319**, structure **47** of **Scheme XIV**, where R^1=H, R^2=chloro, R^3=methyl, X=O). (*R/S*)-9-chloro-1,2-dihydro-5-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (30 mg, 0.092 mmol) was dissolved in methanol (3 mL) and treated with p-toluenesulfonic acid (10 mg). After 10 min the reaction was quenched with $NaHCO_3$ (2 mL). The resulting mixture was diluted with water (2 mL), poured into a separatory funnel, and extracted with EtOAc (3 x 20 mL). The combined organics were washed with NaCl(sat) (1 x 20 mL), dried (Na_2SO_4), filtered, and concentrated onto Celite. The material was purified by flash chromatography on silica (20 g) using 10 % EtOAc:hexanes as eluent to afford 20 mg (64%) of Compound **319** as an opaque oil. Data for Compound **319**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.73 (d, *J* = 2.4, 1H), 7.56 (d, *J* = 8.3, 1H), 7.17 (dd, *J* = 8.2, 2.4, 1H), 7.08 (d, *J* = 8.3, 1H), 6.80 (d, *J* = 8.3, 1H), 6.37 (s, 1H), 5.62 (br s,1H), 5.54 (s, 1H), 3.44 (s, 3H), 2.27 (2, 3H), 1.32 (s, 3H), 1.17 (s, 3H).

EXAMPLE 220

9-Chloro-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **320**, structure **93** of **Scheme XXV**, where R^{1-2}=R^{4-6}=H, R^3=chloro, R^{7-9}=methyl) 6-(5-Chloro-2-hydroxyphenyl)-1,2-dihydro-5-hydroxymethyl-2,2,4-trimethylquinoline (EXAMPLE 219; structure 94 of **Scheme XXV**, where R^{1-2}=R^{4-6}=H, R^3=chloro, R^{7-9} =methyl)(20 mg, 0.061 mmol) was dissolved in CH_2Cl_2 and treated with thionyl chloride (5 μL, 0.067 mmol) and triethylamine (9 μL 0.067 mmol). After 2 h the reaction was quenched with water and poured into a separatory funnel containing CH_2Cl_2 (20 mL) and water (10mL). The aqueous was extracted with CH_2Cl_2 (2 x 20 mL). The combined organics were washed with NaCl (sat)(1 x 15 mL), dried (Na_2SO_4), filtered and concentrated. The resulting benzyl chloride intermediate was dissolved in 1,2-dichloroethane (1mL) and treated with triethylamine (100 mL), then heated to reflux. After 1 h the reaction was quenched with water and poured into a separatory funnel. The pH was adjusted to 6 (1%v/v HCl) and the aqueous was extracted with CH_2Cl_2 (2 x 20 mL) The combined organics were washed with NaCl(sat) (20 mL), dried (Na_2SO_4), filtered, and concentrated onto Celite. The material was purified by flash chromatography on silica gel (20 g) using 5% EtOAc:hexanes to afford 10 mg (53%) of Compound **320.** Data for Compound **320:** **^{1}H NMR** (400 MHz, acetone-d_6) 7.60 (d, *J* = 2.4, 1H), 7.43 (d, *J* = 8.4, 1H), 7.08 (dd, *J* = 8.5,2.4, 1h), 6.89 (d, *J* = 8.5, 1H), 6.70 (d, *J* = 8.4, 1H), 5.56 (br s, 1H), 5.49 (s, 1H), 5.32 (s, 2H), 2.11 (s, 3H), 1.25 (s, 6H).

EXAMPLE 221

(*R/S*)-9-Chloro-1,2-dihydro-2,2,4-trimethyl-5-propyloxy-5*H*-chromeno[3,4-*f*]quinoline (Compound **321**, structure **47** of **Scheme XIV**, where R^1=H, R^2=chloro, R^3=propyl, X=O)

(*R/S*)-9-Chloro-1,2-dihydro-5-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (EXAMPLE 219; structure **46** of **Scheme XIV**, where R^1=H, R^2=chloro) (30 mg, 0.092 mmol) was dissolved in 1-propanol (3 mL) and treated with p-toluenesulfonic acid (10 mg). After 10 min the reaction was quenched with $NaHCO_3$ (2 mL). The resulting mixture was diluted with H_2O (2 mL), poured into a separatory funnel, and extracted with EtOAc (3 x 20 mL). The combined organics were washed with NaCl(sat) (1 x 20 mL), dried (Na_2SO_4), filtered, and concentrated onto celite. The material was purified by flash chromatography on silica (20 g) using 10 % EtOAc:hexanes as eluent to afford 22 mg (61%) of Compound **321** as an opaque oil. Data for Compound **321:** **^{1}H NMR** (400 MHz, acetone-d_6) 7.73 (d, *J* = 2.4, 1H), 7.56 (d, *J* = 8.5, 1H), 7.14 (dd, *J* = 8.3, 2.5, 1H), 7.03 (d, *J* = 8.5, 1H), 6.80 (d, *J* = 8.5, 1H), 6.46 (s, 1H), 5.60 (br s, 1H), 5.53 (s, 1H), 3.81 (m, 1H), 3.59 (m, 1H), 2.29 (s, 3H), 1.46 (m, 2H), 1.32 (s, 3H), 1.17 (s, 3H), 0.75, (m, 3H).

EXAMPLE 222

(*R/S*)-9-Fluoro-1,2-dihydro-5-methoxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **322**, structure **47** of **Scheme XIV**, where R^1=H, R^2=fluoro, R^3=methyl, X=O). This compound was prepared in a manner similar to that described for Compound **319** (EXAMPLE 219) from Compound **207** (55 mg) to afford 34 mg (59%) of Compound **322** as a clear oil. Data for Compound **322**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.53 (d, *J* = 8.5, 1H), 7.48 (dd, *J* = 9.9, 3.0, 1H), 7.05 (dd, *J* = 8.7, 4.9, 1H), 6.92 (m, 1H), 6.80 (d, *J* = 8.3, 1H), 6.34 (s, 1H), 5.54 (d, *J* = 1.4, 1H), 3.44 (s, 3H), 2.28 (d, *J* = 1.4, 3H), 1.32 (s, 3H), 1.16 (s, 3H).

EXAMPLE 223

(*R/S*)-9-Fluoro-1,2-dihydro-2,2,4-trimethyl-5-thiopropoxy-5*H*-chromeno[3,4-*f*]quinoline (Compound **323**, structure **47** of **Scheme XIV**, where R^1=H, R^2=fluoro, R^3=propyl, X=S). (*R/S*)-9-Fluoro-1,2-dihydro-5-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (structure **46** of **Scheme XIV**, where R^1=H, R^2=fluoro). This compound was prepared in a manner similar to that of 9-chloro-1,2-dihydro-5-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (EXAMPLE 219) from Compound **207** (0.16 g, 0.51 mmol) to afford 80 mg (50%) of 9-fluoro-1,2-dihydro-5-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline as a white solid. Data for 9-fluoro-1,2-dihydro-5-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline: **^{1}H NMR** (400 MHz, acetone-d_6) 7.52 (d, *J* = 8.5, 1H), 7.46 (dd, *J* = 9.9, 2.9, 1H), 6.93 (m, 1H), 6.86 (m, 2H), 6.78 (d, *J* = 8.5, 1H), 5.98 (d, *J* = 6.0, 1H), 5.56 (br s, 1H), 5.52 (d, *J* = 1.1, 1H), 2.37 (d, *J* = 1.2, 3H), 1.30 (s, 3H), 1.18 (s, 3H).

(*R/S*)-9-Fluoro-1,2-dihydro-2,2,4-trimethyl-5-thiopropoxy-5*H*-chromeno[3,4-*f*]quinoline (Compound **323**, structure **47** of **Scheme XIV**, where R^1=H, R^2=fluoro, R^3=propyl, X=S). This compound was prepared in a manner similar to that of Compound **319** (EXAMPLE 219) from 9-fluoro-1,2-dihydro-5-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (18 mg) to afford 21 mg (99%) of Compound **323** as a clear oil. Data for Compound **323**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.48 (d, *J* = 8.5, 1H), 7.45 (dd, *J* = 10.0, 1.7, 1H), 7.14 (s, 1H), 6.95 (m, 2H), 6.73 (d, *J* = 8.5, 1H), 5.52 (d, *J* = 1.3, 1H), 2.76 (m, 1H), 2.58 (dt, *J* =

12.9, 7.4, 1H), 2.47 (d, *J* = 1.2, 3H), 1.66 (m, 2H), 1.25 (s, 3H), 1.22 (s, 3H), 0.95 (t, *J* = 7.3, 3H).

EXAMPLE 224

(*R/S*)-9-Fluoro-1,2-dihydro-2,2,4-trimethyl-5-propoxy-5*H*-chromeno[3,4-*f*]quinoline (Compound **324**, structure **47** of **Scheme XIV**, where R^1=H, R^2=fluoro, R^3=propyl, X=O). This compound was prepared in a manner similar to that of Compound **319** (EXAMPLE 219) from 9-fluoro-1,2-dihydro-5-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (EXAMPLE 223) (20 mg) to afford 21 mg (95%) of Compound **324** as a white solid. Data for Compound **324**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.53 (d, *J* = 8.4, 1H), 7.47 (dd, *J* = 9.9, 2.9, 1H), 7.02 (dd, *J* = 8.8, 5.0, 1H), 6.95 (m, 1H), 6.80 (d, *J* = 8.5, 1H), 5.53 (d, *J* = 1.5, 1H), 3.81 (dt, *J* = 9.2, 6.7, 1H), 3.58 (dt, *J* = 9.2, 6.7, 1H), 2.29 (d, *J* = 1.5, 3H), 1.46 (sext, *J* = 6.9, 2H), 1.32 (s, 3H), 1.16 (s, 3H), 0.75 (t, *J* = 7.4, 3H).

EXAMPLE 225

(*R/S*)-5-Butyl-9-chloro-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **325**, structure **42** of **Scheme XI**, where R^1=H, R^2=chloro, R=butyl). This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **209** (38 mg, 0.12 mmol) and 2.5 M *n*-BuLi in hexanes (0.28 mL, 0.70 mmol) to afford 7 mg (16%) of Compound **325** as a clear oil. Data for Compound **325**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.72 (d, *J* = 2.4, 1H), 7.58 (d, *J* = 8.5, 1H), 7.12 (dd, *J* = 8.3, 2.5, 1H), 7.05 (d, *J* = 8.5, 1H), 6.75 (d, *J* = 8.5, 1H), 5.53 (s, 1H), 4.82 (t, *J* = 8.0, 1H), 2.40 (m, 2H), 2.09 (s, 3H), 1.5-1.4 (m, 6H), 1.25 (br s, 6H), 0.95 (t, *J* = 7.8, 3H).

EXAMPLE 226

(*R/S*)-5-Butyl-1,2-dihydro-9-methoxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **326**, structure **42** of **Scheme XI**, where R^1=H, R^2=methoxy, R=butyl). This compound (12 mg, 33%) was obtained as a by-product in the formation of Compound **355** (EXAMPLE 255) as a colorless oil. Data for Compound **326**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.47 (d, *J* = 8.4, 1H), 7.20 (d, *J* = 2.8, 1H), 6.80 (d, *J* = 8.5, 1H), 6.69 (m, 2H), 5.79 (dd, J = 10.3, 3.2, 1H), 5.51 (d, J = 1.2, 1H), 3.80 (s, 3H), 2.24 (d, J = 1.0, 1H), 1.74 (m, 1H), 1.5-1.3 (m, 5H), 1.27 (s, 3H), 1.18 (s, 3H), 0.84 (t, J = 7.5, 3H).

EXAMPLE 227

(*R/S*)-9-Fluoro-1,2-dihydro-2,2,4,5-tetramethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **327**, structure **42** of **Scheme XI**, where R^1=H, R^2=fluoro, R=methyl).

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **207** (36 mg, 0.12 mmol) and 1.4 M MeLi in ether (0.45 mL, 0.63 mmol) to afford 6 mg (16%) of Compound **327** as a clear oil. Data for Compound **327**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.46 (d, J = 8.4, 1H), 7.41 (dt, J = 10.0, 1.5, 1H), 6.84 (m, 2H), 6.80 (d, J = 8.5, 1H), 6.07 (q, J = 6.5, 1H), 5.53 (d, J = 1.4, 1H), 2.25 (d, J = 1.1, 3H), 1.32 (d, J = 6.5, 3H), 1.26 (s, 3H), 1.20 (s, 3H).

EXAMPLE 228

(*R/S*)-9-Fluoro-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **328**, structure **42** of **Scheme XI**, where R^1=R=H, R^2=fluoro).

This compound was prepared in a manner similar to that described for Compound **202** (EXAMPLE 102) from 9-fluoro-1,2-dihydro-5-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (EXAMPLE 223) (15 mg) to afford 14 mg (99%) of Compound **328** as a clear glass. Data for Compound **328**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.41 (d, J = 8.4, 1H), 7.41 (dt, J = 10.0, 1.5, 1H), 6.84 (m, 2H), 6.70 (d, J = 8.4, 1H), 5.49 (d, J = 1.2, 1H), 5.29 (s, 2H), 2.11 (d, J = 1.6, 3H), 1.26 (s, 6H).

EXAMPLE 229

(*R/S*)-1,2-Dihydro-9-methoxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **329**, structure **42** of **Scheme XI**, where R^1=R=H, R^2=methoxy).

(*R/S*)-1,2-Dihydro-5-hydroxy-9-methoxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (structure **46** of **Scheme XIV**, where R^1=H, R^2=methoxy). This compound was prepared in a manner similar to that of 9-chloro-1,2-dihydro-5-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (EXAMPLE 219) from Compound **314** (24 mg, 0.075 mmol) to afford 15 mg (62%) of 1,2-dihydro-5-hydroxy-9-methoxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline as a white solid, which was used directly in the next step.

(*R/S*)-1,2-Dihydro-9-methoxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **329**, structure **42** of **Scheme XI**, where R^1=R=H, R^2=methoxy) This compound was prepared in a manner similar to that described for Compound **202** (EXAMPLE 102) from 1,2-dihydro-5-hydroxy-9-methoxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (15 mg) to afford 12 mg (98%) of Compound **329** as a clear glass. Data for Compound **329**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.41 (d, *J* = 8.3, 1H), 7.16 (d, *J* = 3.0, 1H), 6.81 (d, *J* = 8.6, 1H), 6.68 (m, 1H), 5.48 (d, *J* = 1.2, 1H), 5.23 (s, 2H), 3.80 (s, 3H), 2.10 (d, *J* = 1.2, 3H), 1.24 (s, 6H).

EXAMPLE 230

(*R/S*)-1,2-Dihydro-2,2,4,9-tetramethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **330**, structure **42** of **Scheme XI**, where R^1=R=H, R^2=methyl)

This compound was prepared in a manner similar to Compound **229** (EXAMPLE 229) from Compound **316** (34 mg, 0.11 mmol) to afford 16 mg (50%) of Compound **330** as a clear oil. Data for Compound **330**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.42 (m, 1H), 7.41 (d, *J* = 8.4, 1H), 6.90 (m, 1H), 6.76 (d, *J* = 8.0, 1H), 6.64 (d, *J* = 8.4, H), 5.48 (s, 1H), 5.41 (br s, 1H), 5.25 (s, 2H), 2.30 (s, 3H), 2.11 (d, *J* = 1.4, 3H), 1.24 (s, 6H).

EXAMPLE 231

(*R/S*)-7-Chloro-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **331**, structure **93** of **Scheme XXIV**, where R^1=chloro, R^{2-6}=H, R^{7-9}=methyl)

This compound was prepared in a manner similar to Compound **229** (EXAMPLE 229) from Compound **317** (20 mg, 0.061 mmol) to afford 11 mg (58%) of Compound **331** as a clear oil. Data for Compound **331**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.57 (dd, *J* = 7.9, 1.2, 1H), 7.42 (d, *J* = 8.4, 1H), 7.18 (dd, *J* = 7.9, 1.2, 1H), 6.98 (t, *J* = 7.9, 1H), 6.70 (d, *J* = 8.4, 1H), 5.56 (br s, 1H), 5.50 (d, *J* = 1.2, 1H), 5.40 (s, 2H), 2.14 (d, *J* = 1.3, 3H), 1.25 (s, 6H).

EXAMPLE 232

(*R/S*)-9-Chloro-1,2-dihydro-2,2,4,5-tetramethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound 332, structure **42** of **Scheme XI**, where R^1=H, R^2=chloro, R=methyl)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **209** (40 mg, 0.123 mmol) and methyllithium (438 µl, 0.614 mmol, 1.4 M in ether, Aldrich) to afford 8 mg (20%) of Compound **332** as an opaque oil. Data for Compound **332**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.65 (d, *J* = 2.5, 1h), 7.49 (d, *J* = 8.4, 1H), 7.08 (dd, *J* = 8.5, 2.4, 1H), 6.85 (d, *J* = 8.5, 1H), 6.70 (d, *J* = 8.5, 1H), 6.09 (s, 1H), 5.52 (s, 1H), 2.25 (s, 3H), 1.32 (d, *J* = 6.5, 3H), 1.26 (s, 3H), 1.20 (s, 3H).

EXAMPLE 233

(*R/S*)-5-(4-Bromophenyl)-9-chloro-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound 333, structure **42** of **Scheme XI**, where R=4-bromophenyl, R^1=H, R^2=Cl)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **209** (40 mg, 0.123 mmol) and 1,4-dibromobenzene (203 mg, 0.859 mmol) to afford 11 mg (19%) of Compound **333** as a pale cream colored oil. Data for Compound **333**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.59 (d, *J* = 2.4, 1H), 7.58 (d, *J* = 6.3, 1H), 7.42 (d, *J* = 8.5, 2H), 7.16 (d, *J* = 8.5, 2H), 6.94 (dd, *J* = 8.2, 4.2, 1H), 6.92 (s,1H), 6.84 (d, *J* = 8.4, 1H), 6.77 (d, *J* = 8.4, 1H), 5.68 (br s, 1H), 5.48 (s, 1H), 1.98 (s, 3H), 1.27 (s, 3H), 1.24 (s, 3H).

EXAMPLE 234

(*R/S*)-9-Chloro-5-(3-chlorophenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound 334, structure **42** of **Scheme XI**, where R=3-chlorophenyl, R^1=H, R^2=Cl)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **209** (40 mg, 0.123 mmol) and 3-bromochlorobenzene (164 mg, 0.856 mmol) to afford 9 mg (17%) of Compound **334** as a pale yellow oil. Data for Compound **334**: ^{1}**H NMR** (400 MHz, acetone-d_6) 7.61 (d, *J* = 2.3, 1H), 7.59 (d, *J* = 9.0, 1H), 7.25 (m, 4H), 6.95 (m, 2H), 6.85 (d, *J* = 8.3, 1H), 6.83 (d, *J* = 7.3, 1H), 5.72 (br s, 1H), 5.50 (s, 1H), 2.00 (s, 3H), 1.28 (s, 3H), 1.26 (s, 3H).

EXAMPLE 235

(*R/S*)-9-Chloro-1,2-dihydro-2,2,4-trimethyl-5-(3-methylphenyl)-5*H*-chromeno[3,4-*f*]quinoline (Compound **335**, structure **42** of **Scheme XI**, where R=3-methylphenyl, R^1=H, R^2=Cl)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **209** (20 mg, 0.061 mmol) and 3-bromotoluene (147 mg, 0.859 mmol) to afford 10 mg (41%) of Compound **335** as a pale white oil. Data for Compound **335**: ^{1}**H NMR** (400 MHz, acetone-d_6) 7.59 (d, *J* = 2.4, 1H), 7.58 (d, *J* = 9.1, 1H), 7.19 (m, 2H), 6.95 (m,3H), 6.83 (d, *J* = 8.5, 1H), 6.78 (d, *J* = 8.5, 1H), 5.64 (br s, 1H), 5.81 (s, 1H), 2.20 (s, 3H), 2.05 (s, 3H), 1.27 (s, 3H), 1.24 (s, 3H).

EXAMPLE 236

(*R/S*)-9-Chloro-5-(4-chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **336**, structure **42** of **Scheme XI**, where R=4-chloro-3-methylphenyl, R^1=H, R^2=Cl)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **209** (20 mg, 0.061 mmol) and 5-bromo-2-chlorotoluene (177 mg, 0.859 mmol) to afford 9 mg (34%) of Compound **336** as a cream colored oil. Data for Compound **336**: ^{1}**H NMR** (400 MHz, acetone-d_6) 7.60 (d, *J* = 2.4, 1H), 7.57 (d,*J* = 8.5, 1H), 7.23 (m, 2H), 7.00 (m, 2H), 6.91 (s, 1H), 6.84 (d, *J* = 8.2, 1H), 6.79 (d, *J* = 8.5, 1H), 5.68 (br s, 1H), 5.48 (ds, 1H), 2.23 (s, 3H), 1.99 (s, 3H), 1.27 (s, 3H), 1.25 (s, 3H).

EXAMPLE 237

(*R/S*)-9-Chloro-1,2-dihydro-5-[3-(trifluoromethyl)phenyl]-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound 337, structure **42** of **Scheme XI**, where R=3-(trifluoromethyl)phenyl, R^1=H, R^2=Cl)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **209** (40 mg, 0.123 mmol) and 3-bromobenzotrifluoride (276 mg, 1.23 mmol) to afford 11 mg (20%) of Compound **337** as a cream colored oil. Data for Compound **337**: **^{1}H NMR** (400 MHz, acetone-d$_6$) 7.61 (d, *J* = 2.3, 1H), 7.52 (m, 4H), 7.07 (s, 1H), 6.99 (dd, *J* = 8.5, 2.4, 1H), 6.87 (d, *J* = 8.3, 1H), 6.84 (d, *J* = 8., 1H), 5.73 (br s, 1H), 5.51 (s, 1H), 2.01 (s, 3H), 1.27 (s, 6H).

EXAMPLE 238

(*R/S*)-9-Chloro-5-(3,5-dichlorophenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **338**, structure **42** of **Scheme XI**, where R=3,5-dichlorophenyl, R^1=H, R^2=Cl)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **209** (40 mg, 0.123 mmol) and 1-bromo-3,5-dichlorobenzene (277 mg, 1.23 mmol) using diethyl ether for the formation of the aryl lithium in the first step. The final step afforded 11 mg (20%) of Compound **338** as a pale yellow oil. Data for Compound **338**: **^{1}H NMR** (400 MHz, acetone-d$_6$) 7.64 (d, *J* = 2.3, 1H), 7.61 (d, *J* = 8.5, 1H), 7.32 (s, 1H), 7.20 (s,1H), 7.19 (s, 1H), 7.03 (dd, *J* = 8.9, 2.4, 1H), 6.91 (s, 1H), 6.89 (d, *J* = 6.7, 1H), 6.88 (d, *J* = 6.7, 1H), 5.78 (br s, 1H), 5.53 (s, 1H), 2.03 (s, 3H), 1.28 (s, 3H), 1.27 (s, 3H).

EXAMPLE 239

(*R/S*)-9-Chloro-1,2-dihydro-5-(4-methoxyphenyl)-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **339**, structure **42** of **Scheme XI**, where R= 4-methoxyphenyl, R^1=H, R^2=Cl)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **209** (40 mg, 0.123 mmol) and 4-bromoanisole (230 mg, 1.23 mmol) to afford 11 mg (21%) of Compound **339** as a pale yellow oil. Data for Compound **339**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.59 (d, J = 2.5, 1H), 7.56 (d, J = 8.5, 1H), 7.11 (d, J = 8.7, 2H), 6.94 (dd, J = 8.5, 2.4, 1H), 6.89 (s, 1H), 6.82 (d, J = 8.5, 1H), 6.75 (m, 3H), 5.61 (br s, 1H), 5.45 (s, 1H), 3.69 (s, 3H), 1.99 (s, 3H), 1.26 (s, 3H), 1.23 (s, 3H).

EXAMPLE 240

(*R/S*)-9-Chloro-5-(3-fluoro-4-methoxyphenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **340**, structure **42** of **Scheme XI**, where R=3-fluoro-4-methoxyphenyl, R^1=H, R^2=Cl)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **209** (20 mg, 0.061 mmol) and 4-bromo-2-fluoroanisole (88 mg, 0.429 mmol) to afford 8 mg (29%) of Compound **340** as a pale yellow oil. Data for Compound **340**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.60 (d, J = 2.4, 1H), 7.58 (d, J = 8.5, 1H), 7.02 (dd, J = 10.2, 2.4, 1H), 6.97 (dd, J = 8.5, 2.3, 1H), 6.94 (d, J = 8.5, 1H), 6.90 (s, 1H), 6.89 (m, 1H), 6.84 (d, J = 8.5, 1H), 6.79 (d, J = 8.5, 1H), 5.68 (br s, 1H), 5.48 (s, 1H), 3.79 (s, 3H), 2.00 (s, 3H), 1.27 (s, 3H), 1.24 (s, 3H).

EXAMPLE 241

(*R/S*)-9-Chloro-5-(4-fluorophenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline(Compound **341**, structure **42** of **Scheme XI**, where R=4-fluorophenyl, R^1=H, R^2=Cl)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **209** (40 mg, 0.123 mmol) and 4-fluorophenyl magnesium bromide (1 ml, 1.03 mmol, 1 M, Aldrich) to afford 11 mg (22%) of Compound **341** as a pale yellow oil. Data for Compound **341**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.60 (d, *J* = 2.4, 1H), 7.58 (d, *J* = 7.3, 1H), 7.24 (m, 2H), 6.96 (m, 4H), 6.84 (d, *J* = 8.3, 1H), 5.67 (br s, 1H), 5.48 (s, 1H), 1.98 (s, 3H), 1.26 (s, 3H), 1.24 (s, 3H).

EXAMPLE 242

(*R/S*)-9-Chloro-5-(3-chloro-4-methoxy-5-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **342**, structure **42** of **Scheme XI**, where R=3-chloro-4-methoxy-5-methylphenyl, R^1=H, R^2=Cl)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **209** (40 mg, 0.123 mmol) and 4-bromo-2-chloro-5-methylanisole (181 mg, 0.770 mmol) to afford 12 mg (21%) of Compound **342** as a pale yellow oil. Data for Compound **342**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.61 (d, *J* = 2.4, 1H), 7.58 (d, *J* = 8.4, 1H), 7.03 (m, 1H), 6.99 (dd, *J* = 8.5, 2.4, 2H), 6.91 (s, 1H), 6.84 (dd, *J* = 8.3, 3.8, 2H), 5.69 (br s, 1H), 5.49 (s, 1H), 3.70 (s, 3H), 2.18 (s, 3H), 2.01 (s, 3H), 1.27 (s, 3H), 1.26 (s, 3H).

EXAMPLE 243

(*R/S*)-9-Chloro-5-(4-fluoro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **343**, structure **42** of **Scheme XI**, where R=4-fluoro-3-methylphenyl, R^1=H, R^2=Cl)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **209** (40 mg, 0.123 mmol) and 4-fluoro-3-phenyl magnesium bromide (1 ml, 1.026 mmol, 1M, Aldrich) to afford 8 mg (16%) of Compound **343** as a pale yellow oil. Data for Compound **343**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.59 (d, *J* = 2.6, 1H), 7.57 (d, *J* = 8.6, 1H), 7.12 (d, *J*

= 8.1, 1H), 6.99 (m, 1H), 6.96 (dd, *J* = 8.2, 2.4, 1H), 6.90 (m, 1H), 6.84 (d, *J* = 8.3, 1H), 6.77 (d, *J* = 8.5, 1H), 5.68 (br s, 1H), 5.48 (s, 1H), 2.14 (s, 3H), 1.25 (s, 3H), 1.24 (s, 3H).

EXAMPLE 244

(*R/S*)-9-Chloro-5-(3-fluorophenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **344**, structure **42** of **Scheme XI**, where R=3-fluorophenyl, R^1=H, R^2=Cl)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **209** (40 mg, 0.123 mmol) and 1-bromo-3-fluorobenzene (150 mg, 0.860 mmol) to afford 11 mg (22%) of Compound **344** as a pale yellow oil. Data for Compound **344**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.61 (d, *J* = 2.4, 1H),7.59 (d, *J* = 8.4, 1H), 7.29 (m, 1H), 7.04 (d, *J* = 7.9, 1H), 6.97 (m, 4H), 6.85 (d, *J* = 8.5, 1H), 6.80 (d, *J* = 8.5, 1H), 5.7 (br s, 1H), 5.50 (s, 1H), 2.01 (s, 3H), 1.27 (s, 3H), 1.25 (s, 3H).

EXAMPLE 245

(*R/S*)-1,2-Dihydro-2,2,4-trimethyl-5-[(3,4-methylenedioxy)phenyl]-5*H*-chromeno[3,4]-*f*quinoline (Compound **345**, structure **32** of **Scheme IX**, where R=3,4-(methylenedioxy)phenyl

This compound was prepared by the General Procedure 5 (EXAMPLE 60) from 4-bromo-1,2-(methylenedioxy)benzene (201 mg, 1.0 mmol) and Compound **159** (15 mg, 0.05 mmol) to afford 1.5 mg (8%) of Compound **345** as a colorless oil. Data for Compound **345**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.60 (d, *J* = 7.6, 1 H), 7.55 (d, *J* = 8.4, 1 H), 6.98 (t, *J* = 7.6, 1 H), 6.88-6.60 (m, 6 H), 5.98 (s, 1 H), 5.91 (s, 2 H), 5.51 (bs, 1 H), 5.46 (s, 1 H), 2.02 (s, 3 H), 1.25 (s, 3 H), 1.23 (s, 3 H).

EXAMPLE 246

(*R/S*)-5-(4-Chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4]-*f*quinoline (Compound **346**, structure **32** of **Scheme IX**, where R=4-chloro-3-methylphenyl)

This compound was prepared by the General Method 5 (EXAMPLE 60) from 5-bromo-2-chlorotoluene (206 mg, 1.0 mmol) and Compound **159** (10 mg, 0.03 mmol) to afford 8.0 mg (67%) of Compound **346** as a colorless oil. Data for Compound **346**: **^{1}H NMR** (400 MHz,

acetone-d_6) 7.60 (d, *J* = 7.6, 1 H), 7.55 (d, *J*= 8.4, 1 H), 7.23-7.19 (m, 2 H), 7.01 (d, *J*= 9.9, 1 H), 6.97 (d, *J*= 7.7, 1 H), 6.89 (s, 1 H), 6.88-6.81 (m, 2 H), 6.78 (d, *J* = 8.0, 1 H), 5.55 (bs, 1 H), 5.48 (s, 1 H), 2.22 (s, 3 H), 2.00 (s, 3 H), 1.26 (s, 3 H), 1.24 (s, 3 H).

EXAMPLE 247

(*R/S*)-5-(4-Bromo-3-pyridyl)-1,2,3,4-tetrahydro-2,2-dimethyl-4-methylidene-5*H*-chromeno[3,4-*f*]quinoline (Compound **347**, structure **33** of **Scheme IX**, where R=4-bromo-3-pyridyl).

This compound (1.8 mg, 3%) was obtained as a colorless oil along with Compound **197** as described above (EXAMPLE 97). Data for Compound **347**: **^{1}H NMR** (400 MHz, $CDCl_3$) 8.22 (d, *J* = 5.2, 1 H), 7.56-7.49 (m, 2 H), 7.34 (s, 1 H), 7.12 (d, *J* = 6.5, 1 H), 7.03 (td, *J* = 7.4, 1.3, 1 H), 6.92 (td, *J* = 7.4, 1.3, 1 H), 6.86 (d, *J* = 7.5, 1 H), 6.61 (d, *J* = 8.2, 1 H), 6.58 (s, 1 H), 4.98 (s, 1 H), 4.52 (s, 1 H), 2.43 (d, *J* = 14.5, 1 H), 2.22 (d, *J* = 14.5, 1 H), 1.34 (s, 3 H), 1.17 (s, 3 H).

EXAMPLE 248

(*R/S*)-5-(3,5-Difluorophenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **348**, structure **32** of **Scheme IX**, where R=3,5-difluorophenyl)

This compound was prepared by the General Method 5 (EXAMPLE 60) from 1-bromo-3,5-difluorobenzene (193 mg, 1.0 mmol) and Compound **159** (20 mg, 0.07 mmol) to afford 14 mg (53%) of Compound **348** as a colorless oil. Data for Compound **348**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.63 (d, *J* = 7.6, 1 H), 7.58 (d, *J* = 8.4, 1 H), 7.03 (t, *J* = 7.7, 1 H), 6.95 (s, 1 H), 6.94-6.83 (m, 6 H), 5.62 (bs, 1 H), 5.11 (s, 1 H), 2.04 (s, 3 H), 1.27 (s, 3 H), 1.26 (s, 3 H).

EXAMPLE 249

(*R/S*)-5-(3,5-Dichlorophenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **349**, structure **32** of **Scheme IX**, where R=3,5-dichlorophenyl)

This compound was prepared by the General Method 5 (EXAMPLE 60) from 1-bromo-3,5-dichlorobenzene (226 mg, 1.0 mmol) and Compound **159** (15 mg, 0.05 mmol) to afford 20 mg (95%) of Compound **349** as a colorless oil. Data for Compound **349**: **IR** (neat) 3350,

2940, 1690, 1590, 1480, 1070; **^{1}H NMR** (400 MHz, acetone-d_6) 7.63 (d, *J* = 7.7, 1 H), 7.58 (d, *J* = 8.4, 1 H), 7.29 (t, *J* = 1.9, 1 H), 7.20 (d, *J* = 1.9, 2 H), 7.03 (t, *J* = 7.7, 1 H), 6.97 (s, 1 H), 6.93-6.85 (m, 3 H), 5.63 (bs, 1 H), 5.53 (s, 1 H), 2.04 (s, 3 H), 1.28 (s, 3 H), 1.27 (s, 3 H); **^{13}C NMR** (100 MHz, acetone-d_6) 151.0, 147.3, 145.7, 135.5, 135.1, 135.0, 129.0, 128.8, 128.6, 128.4, 127.8, 125.3, 124.6, 123.2, 123.0, 120.3, 119.7, 118.3, 116.4, 116.3, 74.9, 51.2, 24.0.

EXAMPLE 250

(*R/S*)-5-(3-Bromo-5-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **350**, structure **32** of **Scheme IX**, where R=3-bromo-5-methylphenyl)

This compound was prepared by the General Method 5 (EXAMPLE 60) from 3,5-dibromotoluene (250 mg, 1.0 mmol) and Compound **159** (10 mg, 0.03 mmol) to afford 6.1 mg (46%) of Compound **350** as a colorless oil. Data for Compound **350**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.61 (d, *J* = 7.7, 1 H), 7.56 (d, *J* = 8.4, 1 H), 7.17 (s, 1 H), 7.14 (s, 1 H), 7.10 (s, 1 H), 7.01 (t, *J* = 7.7, 1 H), 6.91 (s, 1 H), 6.90-6.82 (m, 3 H), 5.58 (bs, 1 H), 5.50 (s, 1 H), 2.21 (s, 3 H), 2.02 (s, 3 H), 1.27 (s, 3 H), 1.26 (s, 3 H).

EXAMPLE 251

(*R/S*)-5-(3-Bromo-5-fluorophenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **351**, structure **32** of **Scheme IX**, where R=3-bromo-5-fluorophenyl)

This compound was prepared by the General Method 5 (EXAMPLE 60) from 1,3-dibromo-5-fluorobenzene (254 mg, 1.0 mmol) and Compound **159** (10 mg, 0.03 mmol) to afford 6.2 mg (46%) of Compound **351** as a white powder, along with 0.7 mg (5%) of Compound **352** (EXAMPLE 252). Data for Compound **351**: mp 82-84 °C; **IR** (neat) 3367, 1699, 1595, 1581, 1469, 1435, 1251; **^{1}H NMR** (400 MHz, acetone-d_6) 7.63 (d, *J* = 7.7, 1 H), 7.58 (d, *J* = 8.4, 1 H), 7.23 (d, *J* = 5.2, 1 H), 7.20 (s, 1 H), 7.08-7.02 (m, 2 H), 6.97 (s, 1 H), 6.94-6.85 (m, 3 H), 5.64 (bs, 1 H), 5.53 (s, 1 H), 2.04 (s, 3 H), 1.28 (s, 3 H), 1.27 (s, 3 H); **^{13}C NMR** (100 MHz, acetone-d_6) 163.4 (d, *J* = 250 Hz), 151.1, 147.3, 146.4 (d, *J* = 7.0 Hz), 135.0, 129.1, 128.8, 128.4, 128.3, 125.3, 124.6, 123.2, 123.0, 122.9, 120.4, 119.7, 119.2 (d, *J* = 24.8 Hz), 118.3, 116.4, 115.2 (d, *J* = 22.2 Hz), 74.9, 51.2, 29.4, 24.0.

EXAMPLE 252

(*R/S*)-5-(3-Bromo-5-fluorophenyl)-1,2,3,4-tetrahydro-2,2-dimethyl-4-methylidene-5*H*-chromeno[3,4-*f*]quinoline (Compound **352**, structure **33** of **Scheme IX**, where R=3-bromo-5-fluorophenyl)

The compound (0.7 mg, 5%) was obtained along with Compund **351** as described above (EXAMPLE 251) as a colorless oil. Data for Compound **352**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.54 (d, *J* = 7.7, 1 H), 7.51 (d, *J* = 8.4, 1 H), 7.24 (d, *J* = 5.5, 1 H), 7.06-6.84 (m, 5 H), 6.60 (d, *J* = 8.4, 1 H), 6.57 (s, 1 H), 4.96 (s, 1 H), 4.56 (s, 1 H), 4.01 (bs, 1 H), 2.42 (d, *J* = 12.3, 1 H), 2.21 (d, *J* = 12.3, 1 H), 1.34 (s, 3 H), 1.15 (s, 3 H).

EXAMPLE 253

(*R/S*)-5-[4-Fluoro-3-(trifluoromethyl)phenyl]-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **353**, structure **32** of **Scheme IX**, where R=4-fluoro-3-(trifluoromethyl)phenyl)

This compound was prepared by the General Method 5 (EXAMPLE 60) from 5-bromo-2-fluorobenzotrifluoride (243 mg, 1.0 mmol) and Compound **159** (10 mg, 0.03 mmol) to afford 3.5 mg (27%) of Compound **353** as a colorless oil. Data for Compound **353**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.62 (d, *J* = 7.7, 1 H), 7.61-7.53 (m, 3 H), 7.27 (t, *J* = 7.7, 1 H), 7.04-6.82 (m, 5 H), 5.62 (bs, 1 H), 5.51 (s, 1 H), 2.02 (s, 3 H), 1.26 (s, 6 H).

EXAMPLE 254

(*R/S*)-9-Fluoro-1,2-dihydro-2,2,4-trimethyl-5-(3-methylphenyl)-5*H*-chromeno[3,4-*f*]quinoline (Compound **354**, structure **42** of **Scheme XI**, where R=3-methylphenyl, R^1=H, R^2=F)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **207** (31 mg, 0.10 mmol) and 3-bromotoluene (90 mL, 0.74 mmol) to afford 18 mg (46%) of Compound **354** as a colorless glass. Data for Compound **354**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.53 (d, *J* = 8.5, 1H), 7.33 (dd, *J* = 9.9, 2.9, 1H), 7.08 (m, 2H), 6.98 (d, *J* = 6.7, 2H), 6.89 (s, 1H), 6.83 (d, *J* = 8.5, 1H), 6.75 (m, 2H), 5.48 (s, 1H), 2.20 (s, 3H), 1.99 (s, 3H), 1.27 (s, 3H), 1.25 (s, 3H).

EXAMPLE 255

(*R/S*)-1,2-Dihydro-9-methoxy-2,2,4-trimethyl-5-(3-methylphenyl)-5*H*-chromeno[3,4-*f*]quinoline (Compound **355**, structure **42** of **Scheme XI**, where R=3-methylphenyl, R^1=H, R^2=methoxy)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **314** (32 mg, 0.10 mmol) and 3-bromotoluene (90 mL, 0.74 mmol) to afford 10 mg (25%) of Compound **355** as a colorless glass. Data for Compound **355**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.53 (d, *J* = 8.5, 1H), 7.13 (d, *J* = 2.8, 1H), 7.08 (m, 2H), 6.99 (m, 2H), 6.83 (d, *J* = 6.0, 1H), 6.80 (s, 1H), 6.70 (d, *J* = 8.7, 1H), 6.55 (dd, *J* = 8.7, 2.8, 1H), 5.46 (d, *J* = 1.2, 1H), 3.72 (s, 3H), 2.24 (s, 3H), 1.98 (s, 3H), 1.26 (s, 3H), 1.24 (s, 3H).

EXAMPLE 256

(*R/S*)-9-Fluoro-5-(3-fluoro-4-methoxyphenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **356**, structure **42** of **Scheme XI**, where R=3-fluoro-4-methoxyphenyl, R^1=H, R^2=F)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **207** (41 mg, 0.12 mmol) and 4-bromo-3-fluoroanisole (0.13 mL, 1.0 mmol) to afford 11 mg (20%) of Compound **356** as a yellow oil. Data for Compound **356**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.55 (d, *J* = 8.5, 1H), 7.35 (dd, *J* = 10.0, 2.8, 1H), 7.01 (dd, *J* = 12.5, 1.9, 1H), 6.95 (t, *J* = 6.9, 1H), 6.87 (m, 3H), 6.74 (m, 2H), 5.48 (d, *J* = 1.2, 1H), 3.79 (s, 3H), 1.97 (s, 3H), 1.27 (s, 3H), 1.24 (s, 3H).

EXAMPLE 257

(*R/S*)-9-Fluoro-1,2-dihydro-2,2,4-trimethyl-5-[3-(trifluoromethyl)phenyl]-5*H*-chromeno[3,4-*f*]quinoline (Compound **357**, structure **42** of **Scheme XI**, where R=3-(trifluoromethyl)phenyl, R^1=H, R^2=F)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **207** (40 mg, 0.12 mmol) and 3-bromobenzotrifluoride (0.14 mL, 1.0 mmol) to afford 11 mg (20%) of Compound **357** as a yellow oil. Data for Compound **357**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.54 (d, *J* = 8.5, 1H), 7.35 (dd, *J* = 9.9, 2.9, 1H), 7.10 (m, 2H), 6.98 (d, *J* = 6.7, 2H), 6.89 (s, 1H), 6.85 (d, J = 8.5, 1H), 6.75 (m, 2H), 5.48 (s, 1H), 1.99 (s, 3H), 1.27 (s, 3H), 1.25 (s, 3H).

EXAMPLE 258

(*R/S*)-9-Fluoro-5-(4-fluoro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **358**, structure **42** of **Scheme XI**, where R=4-fluoro-3-methylphenyl, R^1=H, R^2=F)

This compound was prepared by General Method 5 (EXAMPLE 60) from Compound **207** (38 mg, 0.12 mmol) and 1.0 M 4-fluoro-3-methylphenyl magnesium chloride in THF (Aldrich) to afford 25 mg (51%) of Compound **358** as a yellow oil. Data for Compound **358**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.54 (d, J = 8.4, 1H), 7.34 (dd, J = 10.0, 2.8, 1H), 7.14 (m, 1H), 7.00 (m, 1H), 6.91 (d, J = 9.6, 1H), 6.88 (s, 1H), 6.83 (d, J = 8.4, 1H), 6.79-6.68 (m, 2H), 5.48 (s, 1H), 2.13 (s, 3H), 1.99 (s, 3H), 1.27 (s, 3H), 1.24 (s, 3H).

EXAMPLE 259

(*Z*)-5-(2,4-Difluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **359**, structure **45** of **Scheme XIII**, where R^1=R^2=H, R^3=2,4-difluorophenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from 2,4-difluorobenzyl bromide (0.27 ml, 2.10 mmol) and compound **159** (20 mg, 0.07 mmol) to afford 16 mg (56%) of Compound **359** as a yellow oil. Data for Compound **359**: Rf=0.44 (silica gel, 25% EtOAc:hex); **^{1}H NMR** (400 MHz, acetone-d_6) 8.43 (m, 1H), 7.86 (d, J = 8.5, 1 H), 7.67 (d, J = 8.5, 1 H), 7.20 (m, 2 H), 7.11 to 7.03 (m, 3 H), 6.86 (d, J = 8.5, 1 H), 5.88 (s, 1 H), 5.55 (s, 1 H), 2.11 (s, 3 H), 1.29 (brs, 6 H).

EXAMPLE 260

(*Z*)-5-(3,4-Difluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **360**, structure **45** of **Scheme XIII**, where R^1=R^2=H, R^3=3,4-difluorophenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from 3,4-difluorobenzyl bromide (0.27 ml, 2.10 mmol) and Compound **159** (20 mg, 0.07 mmol) to afford 20 mg (70%) of Compound **360** as a yellow oil. Data for Compound **360**: Rf=0.44 (silica gel, 25% EtOAc:hex); **^{1}H NMR** (400 MHz, acetone-d_6) 7.83 (m, 2 H), 7.66 (d, J =

8.5, 1 H), 7.55 (m, 1 H), 7.31 (m, 1 H), 7.24 (m, 2 H), 7.10 (m, 1 H), 6.85 (d, *J* = 8.5, 1 H), 5.67 (s, 1 H), 5.55 (s, 1 H), 2.08 (s, 3 H), 1.28 (brs, 6 H).

EXAMPLE 261

(Z)-5-(3-Fluorobenzylidene)-1,2,3,4-tetrahydro-2,2,4-trimethyl-*5H*-chromeno[3,4-*f*]quinoline (Compound 361, structure xx of Scheme XXX, where R^1=R^2=H, R^3=3-difluorophenyl)

A solution of Compound **159** (20 mg, 0.07 mmol) in EtOAc (10 ml) was stirred over 10% Pd/C (5 mg) at rt under an atmosphere of H_2 (1 atm) for 15 h. The reaction mixture was filtered then concentrated *in vacuo* to afford 14 mg (70%) of the 1,2,3,4-tetrahydro-2,2,4-trimethyl-*5H*-coumarino[3,4-*e*]quinoline as a yellow solid. According to General Method 6 (EXAMPLE 119), from 3-fluorobenzyl chloride (0.17 ml, 1.40 mmol) and 1,2,3,4-tetrahydro-2,2,4-trimethyl-*5H*-coumarino[3,4-*e*]quinoline (14 mg, 0.05 mmol) was obtained 8.6 mg (46%) of Compound **361** as a yellow solid. Data for Compound **361**: Rf=0.38 (silica gel, 25% EtOAc:hex); **^{1}H NMR** (400 MHz, acetone-d_6) 7.82 (d, *J* = 8.5, 1 H), 6.69 (m, 1 H), 7.62 (d, *J* = 8.5, 1 H), 7.58 (d, *J* = 8.5, 1 H), 7.40 (m, 1 H), 7.22 (m, 2 H), 7.08 (m, 1 H), 6.97 (m, 1 H), 6.74 (d, *J* = 8.5, 1 H), 6.24 (s, 1 H), 5.30 (brs, 1 H), 3.76 (m, 1 H). 1.97 (m, 1 H), 1.55 (m, 1 H), 1.40 (d, *J* = 6.6, 3 H), 1.30 (s, 3 H), 1.26 (s, 3 H).

EXAMPLE 262

(Z)-5-(2,6-Difluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-*5H*-chromeno[3,4-*f*]quinoline (Compound 362, structure 45 of Scheme XIII, where R^1=R^2=H, R^3=2,6-difluorophenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from α-bromo-2,3-difluorotoluene (0.43 g, 2.1 mmol) and Compound **159** (20 mg, 0.07 mmol) to afford 4.4 mg (16%) of Compound **362** as a yellow oil. Data for Compound **362**: Rf=0.45 (silica gel, 25% EtOAc:hex); **^{1}H NMR** (400 MHz, acetone-d_6) 7.83(d, *J* = 8.5, 1 H), 7.68 (d, *J* = 8.5, 1 H), 7.35 (m, 1 H), 7.15 (m, 1 H), 7.04 (m, 3 H), 6.90 (d, *J* = 8.5 H, 1 H), 6.87 (d, *J* = 8.5, 1 H), 5.61 (s, 1 H), 5.57 (s, 1 H), 2.23 (s, 3 H), 1.32 (brs, 6 H).

EXAMPLE 263

(Z)-1,2,-Dihydro-5-(2-methylbenzylidene)-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound 363, structure 45 of **Scheme XIII**, where $R^1=R^2=H$, R^3=2-methylphenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from α-chloro-*o*-xylene (0.20 ml, 1.6 mmol) and Compound **159** (15 mg, 0.05 mmol) to afford 15 mg (76%) of Compound **363** as a yellow oil. Data for Compound **363**: Rf=0.45 (silica gel, 25% EtOAc:hex); **^{1}H NMR** (400 MHz, acetone-d_6) 8.22(d, *J* = 8.5, 1 H), 7.82 (d, *J* = 8.5, 1 H), 7.64 (d, *J* = 8.5, 1 H), 7.26 to 7.04 (m, 6 H), 6.83 (d, *J* = 8.5, 1 H), 5.94 (s, 1 H), 5.54 (s, 1 H), 2.28 (s, 3 H), 2.15 (s, 3 H), 1.25 (brs, 6 H).

EXAMPLE 264

(Z)-1,2,-Dihydro-5-(2,4,6-trimethylbenzylidene)-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound 364, structure 45 of **Scheme XIII**, where $R^1=R^2=H$, R^3=2,4,6-trimethylphenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from α-chloroisodurene (0.50 g, 3.0 mmol) and Compound **159** (30 mg, 0.10 mmol) to afford 20 mg (50%) of Compound **364** as a yellow oil. Data for Compound **364**: Rf=0.40 (silica gel, 25% EtOAc:hex); **^{1}H NMR** (400 MHz, $CDCl_3$) 7.65 (d, *J* = 8.5, 1 H), 7.51 (d, *J* = 8.5, 1 H), 7.15 (t, *J* = 8.5, 1 H), 6.93 (t, *J* = 8.5, 1 H), 6.88 (s, 2 H), 6.80 (d, *J* = 8.5, 1 H), 6.65 (d, *J* = 8.5, 1 H), 5.69 (s, 1 H), 5.50 (s, 1 H), 3.73 (brs, 1 H), 2.28 (s, 6 H), 2.26 (s, 3 H), 2.16 (s, 3 H), 1.45 (brs, 6 H).

EXAMPLE 265

(Z)-9-Chloro-5-(2,5-difluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound 365, structure 45 of **Scheme XIII**, where R^1=H, R^2=Cl, R^3=2,5-difluorophenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from Compound **209** (40 mg, 0.123 mmol) and a-bromo-2,5-difluorotoluene (414 mg, 2.0 mmol) to afford 10 mg (19%) of Compound **365** as a yellow oil. Data for Compound **365**: **^{1}H NMR** (400 MHz, acetone-d_6) 8.05 (m, 1H), 7.87 (s,1H), 7.72 (d, *J* = 8.5, 1H), 7.26 (m, 1H), 7.19 (m, 1H), 7.06 (m, 1H), 6.90 (d, *J* = 8.5, 1H), 5.94 (s, 1H), 5.57 (s, 1H), 2.11 (s, 3H), 1.32 (br s, 6H).

EXAMPLE 266

(Z)-5-Benzylidene-9-chloro-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **366**, structure **45** of Scheme **XIII**, where R^1=H, R^2=Cl, R^3=phenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from Compound **209** (40 mg, 0.123 mmol) and benzyl magnesium chloride (614 µL, 0.614 mmol, 1M, Aldrich) to afford 10 mg (20%) of Compound **366** as a yellow oil. Data for Compound **366:** ^{1}**H NMR** (400 MHz, acetone-d_6) 7.83 (d, *J* =2.3, 1H), 7.81 (m, 2H), 7.67 (d, *J* = 8.4, 1H), 7.39 (m, 2H), 7.21 (m, 3H), 6.84 (d, *J* = 8.5, 1H), 5.71 (s, 1H), 2.10 (s, 3H), 1.34 (br s, 6H).

EXAMPLE 267

(Z)-9-Chloro-1,2-dihydro-2,2,4-trimethyl-5-(2-methylbenzylidene)-5*H*-chromeno[3,4-*f*]quinoline (Compound **367**, structure **45** of Scheme **XIII**, where R^1=H, R^2=Cl, R^3=2-methylphenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from Compound **209** (50 mg, 0.154 mmol) and α-chloro-*o*-xylene (345 mg, 2.46 mmol) to afford 14 mg (22%) of Compound **366** as a yellow oil. Data for Compound **366**: ^{1}**H NMR** (400 MHz, acetone-d_6) 7.85 (d, *J* = 2.5, 1H), 7.66 (d, *J* = 8.5, 1H), 7.17 (m, 2H), 7.11 (m, 2H), 6.80 (d, *J* = 8.5, 2H), 6.55 (s, 1H), 5.73 (s, 1H),4.98 (s, 1H), 2.19 (s, 3H), 1.29 (br s, 3H), 1.21 (s, 3H).

EXAMPLE 268

(Z)-5-Benzylidene-9-chloro-1,2-dihydro-2,2-dimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **368**, structure **95** of Scheme **XXVI**, where R^{1-2}=R^{4-6}=R^9=H, R^7=R^8=methyl, R^{10}=phenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from Compound **313** (25 mg, 0.080 mmol) and benzyl magnesium chloride (0.802 mL, 0.802 mmol, 1 M solution in ether, Aldrich) to afford 5 mg (16%) of Compound **368** as a yellow oil. Data for Compound **368:** ^{1}**H NMR** (400 MHz, acetone-d_6) 7.86 (d, *J* = 7.1, 1H), 7.79 (d, *J* = 2.2, 1H), 7.63 (d, *J* = 8.5, 1H), 7.40 (m, 2H), 7.20 (m, 4H), 6.89 (d, *J* = 8.6, 1H), 6.78 (d, *J* = 8.4, 1H), 5.99 (s, 1H), 5.70 (d, *J* = 8.3, 1H), 1.37 (s, 6H).

EXAMPLE 269

(Z)-9-Chloro-5-(2-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound 369, structure **45** of **Scheme XIII**, where R^1=H, R^2=Cl, R^3=2-fluorophenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from Compound **209** (40 mg, 0.123 mmol) and 2-fluorobenzylbromide (160 mg, 0.860 mmol) to afford 9 mg (18%) of Compound **369** as a yellow oil. Data for Compound **369:** ^{1}**H NMR** (400 MHz, acetone-d$_6$) 8.32 (m, 1H), 7.84 (d, *J* = 1.7, 1H), 7.69 (d, *J* = 8.5, 1H), 7.26 (m, 2H), 7.20 (d, *J* = 3.0, 1H), 7.18 (m, 2H), 6.87 (d, *J* = 8.5, 1H), 5.97 (s, 1H), 5.57 (s, 1H), 2.11 (s, 3H), 1.33 (br s, 6H).

EXAMPLE 270

(Z)-9-Chloro-5-(3-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound 370, structure **45** of **Scheme XIII**, where R^1=H, R^2=Cl, R^3=3-fluorophenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from Compound **209** (38 mg, 0.12 mmol) and 3-fluorobenzyl chloride (0.23 mL, 1.9 mmol) to afford 20 mg (42%) of Compound **370** as a yellow oil. Data for Compound **370:** ^{1}**H NMR** (400 MHz, acetone-d$_6$) 7.85 (d, *J* = 2.3, 1H), 7.69 (d, *J* = 8.5, 1H), 7.66 (m, 1H), 7.52 (d, *J* = 7.7, 1H), 7.41 (m, 1H), 7.25 (m, 2H), 7.01 (m, 1H), 6.87 (d, *J* = 8.4, 1H), 5.73 (s, 1H), 5.57 (d, *J* = 1.2, 1H), 1.45-1.35 (br d, 6H). The C(4) methyl is obscured by the acetone multiplet.

EXAMPLE 271

(*E/Z*)-5-Benzylidene-9-fluoro-1,2-dihydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound 371, structure **45** of **Scheme XIII**, where R^1=H, R^2=F, R^3=phenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from Compound **207** (79 mg, 0.25 mmol) and 1.0 M benzylmagnesium chloride in Et$_2$O (Aldrich) to afford 20 mg (19%) of Compound **371** as a yellow oil, as a 2:1 *Z/E* mixture. Data for Compound (*Z*)-**371:** ^{1}**H NMR** (400 MHz, acetone-d$_6$) 7.80 (d, *J* = 7.7, 1H), 7.6 (m, 2H), 7.39 (t, *J* = 7.8, 1H), 7.23 (m, 2H), 7.15 (m, 1H), 7.08 (m, 1H), 6.95 (m, 1H), 6.83 (dd, *J* = 8.4, 2.8, 1H), 5.70 (s, 1H), 5.55 (d, J = 1.2, 1H), 2.10 (s, 3H), 1.35-1.25 (br d, 6H). The characteristic signals for (E)-**371** are: 6.53 (s, 1H), 5.04 (s, 1H), 1.94 (d, J = 1.2, 3H), 1.33 (s, 3H), 1.00 (s, 3H).

EXAMPLE 272

(Z)-5-Benzylidene-8-fluoro-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound **372**, structure **45** of **Scheme XIII**, where R^1=F, R^2=H, R^3=phenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from Compound **208** (55 mg, 0.18 mmol) and 1.0 M benzylmagnesium chloride in Et_2O (Aldrich) to afford 11 mg (17%) of Compound **372** as a yellow oil. Data for Compound **372**: **^{1}H NMR** (400 MHz, acetone-d$_6$) 7.86 (dd, J = 8.7, 6.2, 1H), 7.80 (d, J = 7.6, 2H), 7.61 (d, J = 8.4, 1H), 7.40 (app t, J = 7.8, 2H), 7.20 (m, 1H), 7.05 (m, 1H), 6.86 (m, 1H), 6.83 (d, J = 8.4, 1H), 5.71 (s, 1H), 5.55 (d, J = 1.1, 1H), 2.11 (s, 3H), 1.40 (br s, 6H).

EXAMPLE 273

(Z)-5-Benzylidene-1,2-dihydro-9-methoxy-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound **373**, structure **45** of **Scheme XIII**, where R^1=H, R^2=methoxy, R^3=phenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from Compound **314** (55 mg, 0.18 mmol) and 1.0 M benzylmagnesium chloride in Et_2O (Aldrich) to afford 11 mg (17%) of Compound **373** as a yellow oil. Data for Compound **373**: **^{1}H NMR** (400 MHz, acetone-d$_6$) 7.79 (d, J = 7.6, 2H), 7.53 (d, J = 8.5, 1H), 7.4-7.2 (m, 5H), 6.84 (m, 2H), 5.67 (s, 1H), 5.55 (s, 1H), 3.82 (s, 3H), 2.11 (s, 3H), 1.35-1.30 (br s, 6H).

EXAMPLE 274

(Z)-9-Fluoro-1,2-dihydro-2,2,4-trimethyl-5-(2-methylbenzylidene)-5H-chromeno[3,4-f]quinoline (Compound **374**, structure **45** of **Scheme XIII**, where R^1=H, R^2=fluoro, R^3=2-methylphenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from Compound **207** (34 mg, 0.11 mmol) and freshly prepared 1.0 M 2-methylbenzyl magnesium chloride in Et_2O to afford 30 mg (70%) of Compound **374** as a yellow oil. Data for Compound **374**: **^{1}H NMR** (400 MHz, acetone-d$_6$) 8.20 (d, J = 7.9, 1H), 7.64 (d, J = 8.5, 1H), 7.58 (dd, J =

10.0, 2.9, 1H), 7.26 (app t, *J* = 7.6, 1H), 7.19 (d, *J* = 7.4, 1H), 7.14 (m, 2H), 6.94 (m, 1H), 6.84 (d, *J* = 8.5, 1H), 5.95 (s, 1H), 5.55 (d, *J* = 1.1, 1H), 2.28 (s, 3H), 2.14 (d, *J* = 1.1, 3H), 1.35-1.30 (br s, 6H).

EXAMPLE 275

(*Z*)-8-Fluoro-1,2-dihydro-2,2,4-trimethyl-5-(2-methylbenzylidene)-5*H*-chromeno[3,4-*f*]quinoline (Compound **375**, structure **45** of **Scheme XIII**, where R^1=fluoro, R^2=H, R^3=2-methylphenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from Compound **208** (31 mg, 0.10 mmol) and freshly prepared 1.0 M 2-methylbenzyl magnesium chloride in Et_2O to afford 32 mg (80%) of Compound **375** as a yellow oil. Data for Compound **375**: **^{1}H NMR** (400 MHz, acetone-d_6) 8.19 (d, *J* = 7.9, 1H), 7.86 (dd, *J* = 8.8, 4.2, 1H), 7.61 (d, *J* = 8.5, 1H), 7.28 (app t, *J* = 7.6, 1H), 7.20 (d, *J* = 6.9, 1H), 7.15 (m, 1H), 6.94 (dd, *J* = 9.6, 2.7, 1H), 6.86 (m, 2H), 5.97 (s, 1H), 5.55 (d, *J* = 1.2, 1H), 2.28 (s, 3H), 2.14 (s, 3H), 1.35 (br s, 6H).

EXAMPLE 276

(*Z*)-1,2-Dihydro-9-methoxy-2,2,4-trimethyl-5-(2-methylbenzylidene)-5*H*-chromeno[3,4-*f*]quinoline (Compound **376**, structure **45** of **Scheme XIII**, where R^1=H, R^2=methoxy, R^3=2-methylphenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from Compound **314** (55 mg, 0.18 mmol) and 1.0 M benzylmagnesium chloride in Et_2O (Aldrich) to afford 11 mg (17%) of Compound **373** as a yellow oil. Data for Compound **373**: **^{1}H NMR** (400 MHz, acetone-d_6) 8.23 (d, *J* = 7.8, 1H), 7.64 (d, *J* = 8.5, 1H), 7.37 (m, 1H), 7.30 (m, 1H), 7.15 (m, 2H), 7.04 (d, *J* = 8.6, 1H), 6.82 (d, *J* = 8.4, 1H), 6.77 (dd, *J* = 8.6, 3.0, 1H), 5.92 (s, 1H), 5.53 (d, *J* = 1.2, 1H), 3.82 (s, 3H), 2.27 (s, 3H), 2.14 (s, 3H), 1.35 (br s, 6H).

EXAMPLE 277

(*Z*)-5-Benzylidene-9-fluoro-1,2-dihydro-2,2,4,11-tetramethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **377**, structure **95** of **Scheme XXVI**, where R^{1-2}=R^4=R^6=H, R^3=F, R^5=R^{7-9}=methyl, R^{10}=phenyl)

This compound was prepared by General Method 6 (EXAMPLE 119) from Compound **315** (28 mg, 0.087 mmol) and 1.0 M benzylmagnesium chloride in Et_2O (Aldrich) to afford 19 mg (56%) of Compound **377** as a yellow foam. Data for Compound **377**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.79 (d, J = 7.6, 2H), 6.63 (dd, J = 11.4, 2.9, 1H), 7.39 (app t, J = 7.8, 2H), 7.25 (m, 2H), 6.97 (m, 1H), 6.68 (s, 1H), 5.74 (s, 1H), 5.52 (d, J = 1.2, 1H), 2.61 (s, 3H), 1.97 (s, 3H), 1.33 (br s, 6H).

EXAMPLE 278

(*R/S*)-5-(4-Chlorophenyl)-1,2,3,4-tetrahydro-2,2-dimethyl-5*H*-chromeno[3,4-*f*]-4-quinolinone (Compound **378**, structure **97** of **Scheme XXVII**, where R=4-chlorophenyl)

To a solution of Compound **164** (EXAMPLE 64) (220 mg, 0.6 mmol) in 6 mL of THF at -78 °C was added 1.6 M *n*-BuLi hexane solution (1 mL, 1.6 mmol), followed by di-*t*-butyl dicarbonate (0.7 g, 3.2 mmol) in 2 mL of THF. The reaction mixture was warmed to rt and stirred for 15 h, then was quenched with 2% NaOH aqueous solution. The mixture was extracted with EtOAc (2 x 30 mL) and was concentrated. Chromatography of the crude residue on a silica gel column using 10 % EtOAc/hexane as solvent afforded the N-Boc Compound **164** (87 mg) in 30 % yield in addition to 60 % of the starting material (132 mg). The N-Boc material (40 mg, 0.082 mmol) in methanol (20 mL) at -78 °C was treated with O_3 for 3 min and then with methyl sulfide (0.5 mL) for 30 min. Removal of solvent and chromatography of the crude mixture afforded a colorless oil, which was treated with excess TFA (0.5 mL) in 1 mL of CH_2Cl_2 for 60 min. The reaction was quenched with 2% NaOH (5 mL) and was extracted with EtOAc (2 x 30 mL). Removal of the solvent and chromatography again provided 15 mg (47%) of Compound **378** as a yellow oil. Data for Compound **378**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.86 (d, J = 8.8, 1 H), 7.61 (d, J = 7.7, 1 H), 7.40 (s, 1 H), 7.04 (t, J = 7.7, 1 H), 6.99 (d, J = 8.8, 1 H), 6.90 (t, J = 7.7, 1 H), 6.82 (d, J = 7.7, 1 H), 6.38 (bs, 1 H), 2.65 (d, J = 15.2, 1 H), 2.44 (d, J = 15.2, 1 H), 1.97 (s, 3 H), 1.37 (s, 3 H), 1.27 (s, 3 H).

EXAMPLE 279

(*R*/*S*)-5-(4-Chlorophenyl)-1,2,3,4-tetrahydro-2,2,3,3-tetramethyl-5*H*-chromeno[3,4-*f*]-4-quinolinone (Compound 379, structure **98** of **Scheme XXVIII**, where R=4-chlorophenyl, R^1=methyl).

To a suspension of 40% NaH in mineral oil (10 mg, 0.25 mmol) in THF (1 mL) was added a solution of (*R*/*S*)-1-(*t*-butoxycarbonyl)-5-(4-chlorophenyl)-1,2,3,4-tetrahydro-2,2-dimethyl-5*H*-chromeno[3,4-*f*]-4-quinolinone (structure 96 of **Scheme XXVIII**, where R=4-chlorophenyl, R^1=methyl) (10 mg, 0.02 mmol) and excess MeI (0.1 mL). The reaction was stirred at rt for 2 h and was quenched with water (1 mL), and extracted with EtOAc (2 x 5 mL). Removal of solvent provided the crude mixture, which was treated with TFA (0.2 mL) in dichloromethane (1 mL) for 60 min. Chromatography of the crude mixture on a silica gel column using 15 % EtOAc/Hexane as solvent afforded 6.5 mg (78%) of Compound **379** as a colorless oil. Data for Compound **379**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.73 (d, *J* = 8.7, 1 H), 7.49 (d, *J* = 7.7, 1 H), 7.30 (s, 1 H), 7.13 (s, 4 H), 7.04 (t, *J* = 7.7, 1 H), 6.91 (t, *J* = 7.7, 1 H), 6.83 (d, *J* = 7.7, 1 H), 6.71 (d, *J* = 8.7, 1 H), 4.28 (s, 1 H), 1.29 (s, 3 H), 1.20 (s, 3 H), 1.13 (s, 3 H), 1.03 (s, 3 H).

EXAMPLE 280

(*R*/*S*)-5-(4-Chlorophenyl)-1,2-dihydro-2,2-dimethyl-5*H*-chromeno[3,4-*f*]-4-quinoline (Compound **380**, structure **1A** of **Scheme XXIX**, where R=4-chlorophenyl)

To a solution of Compound **379** (EXAMPLE 279) (10 mg, 0.025 mmol) in toluene (1 mL) at -78 °C was added 0.5 M DIBAL toluene solution (0.1 mL, 0.05 mmol) and the resulting mixture was warmed up to rt. The reaction mixture was quenched with water (1 mL) and was extracted with EtOAc (2 x 5 mL). Removal of solvent and chromatography of the mixture on a silica gel column afforded 6.8 mg (70%) of 5-(4-chlorophenyl)-1,2,3,4-tetrahydro-4-hydroxy-2,2-dimethyl-5*H*-chromeno[3,4-*f*]quinoline as a colorless oil, which was treated in dichloromethane (1 mL) with a catalytic amount of TsOH for 3 h to provide 4.1 mg (63%) of Compound **380** as a colorless oil. Data for Compound **380**: **^{1}H NMR** (400 MHz, acetone-d_6) 7.60 (d, *J* = 7.7, 1 H), 7.52 (d, *J* = 8.5, 1 H), 7.27 (d, *J* = 8.6, 2 H), 7.25 (d, *J* = 8.6, 2 H), 7.01 (t, *J* = 7.7, 1 H), 6.89 (t, *J* = 7.7 Hz, 1 H), 6.81 (d, *J* = 7.7, 1 H), 6.67 (d, *J* = 8.5, 1 H), 6.57 (s, 1 H), 6.33 (d, *J* = 10.0, 1 H), 5.57 (d, *J* = 10.0, 1 H), 5.55 (bs, 1 H), 1.32 (s, 3 H), 1.30 (s, 3 H).

EXAMPLE 281

(+)-(*R*-4l,5l*)-5-(4-Chlorophenyl)-1,2,3,4-tetrahydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]-3-quinolinone (Compound **381**, structure **53** of **Scheme XV**, where R=4-chlorophenyl, R^1=R^2=H)

This compound (0.7 mg) was prepared by HPLC separation of the enantiomers of Compound **381** by a chiral column, Chiracel OD-R, using a 9:1 mixture of methanol and water as mobile phase. The optical purity of Compound **381** was determined by HPLC to be > 90% e.e.; [a]$^{20}{}_{D}$ = + 101 (MeOH).

EXAMPLE 282

(-)-(*R*-4l,5l*)-5-(4-Chlorophenyl)-1,2,3,4-tetrahydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]-3-quinolinone (Compound **382**, structure **53** of **Scheme XV**, where R=4-chlorophenyl, R^1=R^2=H)

This compound (1.5 mg)was prepared by HPLC separation of the enantiomers of Compound **235** by a chiral column, Chiracel OD-R, using a 9:1 mixture of methanol and water as mobile phase. The optical purity of Compound **382** was determined by HPLC to be 68% e.e.; [a]$^{20}{}_{D}$ = - 63 (MeOH).

EXAMPLE 283

(*R*/*S*)-5-(4-Chlorophenyl)-1,2,3,4-tetrahydro-2,2-dimethyl-5*H*-chromeno[3,4-*f*]-3-quinolinone (Compound **383**, structure **4A** of **Scheme XXIX**, where R=4-chlorophenyl)

This compound (0.63 mg, 3%) was prepared in a manner similar to that described for Compound **234** (EXAMPLE 134) from Compound **380** (EXAMPLE 280) as a colorless oil. The major product (41%) was Compound **378** (EXAMPLE 278). Data for Compound **383**: **^{1}H NMR** (400 MHz, CDCl$_3$) 7.62 (d, *J* = 8.3, 1 H), 7.60 (d, *J* = 7.7, 1 H), 7.17 (d, *J* = 8.6, 2 H), 7.09 (d, *J* = 8.6, 2 H), 7.06 (t, *J* = 7.7, 1 H), 6.94 (t, *J* = 7.7, 1 H), 6.83-6.80 (m, 2 H), 6.26 (s, 1 H), 3.88 (bs, 1 H), 3.55 (d, *J* = 20.0, 1 H), 3.11 (d, *J* = 10.0, 1 H), 1.33 (s, 3 H), 1.32 (s, 3 H).

EXAMPLE 284

(*R/S*)-3-(3-Fluorobenzyl)-5-(3-fluorobenzylidene)-1,2,3,4-tetrahydro-3-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **384**, structure **8A** of **Scheme XXX**, where R1=R2=H, R3=3-fluorophenyl)

(*R/S*)-1,2,3,4-Tetrahydro-2,2,4-trimethylcoumarino[3,4-*f*]-3-quinolinone (structure **7A** of **Scheme XXX**, where R^1=R^2=H). This compound was prepared by the same Boc-protection/hydroboration/oxidation/deprotection procedure as described in the synthesis of Compound **234** (EXAMPLE 134) from Compound **159** (EXAMPLE 59) (440 mg, 2.0 mmol) to afford 98 mg (16%) of (*R/S*)-1,2,3,4-tetrahydro-2,2,4-trimethylcoumarino[3,4-*f*]-3-quinolinone as a yellowish oil. Data for (*R/S*)-1,2,3,4-tetrahydro-2,2,4-trimethylcoumarino[3,4-*f*]-3-quinolinone: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.95 (d, *J* = 8.6, 2 H), 7.38 (t, *J* = 8.2, 1 H), 7.31-7.24 (m, 2 H), 7.16 (d, *J* = 8.5, 1 H), 5.29 (q, *J* = 7.4, 1 H), 3.94 (bs, 1 H), 1.56 (s, 3 H), 1.48 (d, *J* = 7.4, 3 H), 1.22 (s, 3 H).

(*R/S*)-3-(3-Fluorobenzyl)-5-(3-fluorobenzylidene)-1,2,3,4-tetrahydro-3-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **384**, structure **8A** of **Scheme XXX**, where R1=R2=H, R3=3-fluorophenyl) To a solution of (*R/S*)-1,2,3,4-tetrahydro-2,2,4-trimethylcoumarino[3,4-*f*]-3-quinolinone (3 mg, 0.01 mmol) in ether (3 mL) at rt was added the freshly prepared a 0.5 M 3-fluorobenzylmagnisium chloride ether solution (0.5 mL, 0.25 mmol) and the resulting mixture was stirred at rt for 2 h, then was quenched with water (5 mL). The mixture was extracted with EtOAc (2 x 5 mL) and was concentrated and purified by silica gel chromatography to afford the intermediate, which was treated with TsOH (5 mg) in dichloromethane (1 mL) for 60 min. The reaction was quenched with 2% NaOH (5 mL) and was extracted with EtOAc (2 x 5 mL). Removal of solvent and chromatography of the mixture afforded 3.0 mg (59%) of Compound **384** as a colorless oil. Data for Compound **384**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.71 (d, *J* = 7.8, 1 H), 7.63 (d, *J* = 11.0, 1 H), 7.51 (d, *J* = 8.4, 1 H), 7.40 (d, *J* = 7.8, 1 H), 7.33 (td, *J* = 7.8, 6.2, 1 H), 7.28-7.18 (m, 3 H), 7.13-6.92 (m, 5 H), 6.65 (d, *J* = 8.3, 1 H), 5.89 (s, 1 H), 3.73 (q, *J* = 6.8, 1 H), 3.66 (s, 1 H), 3.08 (d, *J* = 14.2, 1 H), 2.97 (d, *J* = 14.2, 1 H), 2.79 (s, 1 H), 1.33 (s, 3 H), 1.29 (d, *J* = 6.8, 3 H), 1.18 (s, 3 H).

EXAMPLE 285

(*R/S*)-3,5-Dibutyl-1,2,3,4-tetrahydro-3-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound 385, structure 9A of Scheme XXXI, where R^1=R^2=H, R^3=*n*-butyl)

To a solution of (*R/S*)-1,2,3,4-tetrahydro-2,2,4-trimethylcoumarino[3,4-*f*]-3-quinolinone (EXAMPLE 284) (4 mg, 0.01 mmol) in ether (3 mL) at rt was added 1.6 M *n*-BuLi hexane solution (0.05 mL, 0.08 mmol) and the resulting mixture was stirred at rt for 2 h, then was quenched with water (5 mL). The mixture was extracted with EtOAc (2 x 5 mL) and was concentrated and purified by silica gel chromatography to afford the intermediate, which was treated with Et_3SiH (0.05 mL) and TFA (0.05 mL) in dichloromethane (1 mL) for 60 min. The reaction was quenched with 2% NaOH (5 mL) and was extracted with EtOAc (2 x 5 mL). Removal of solvent and chromatography of the mixture afforded 0.8 mg (20%) of Compound **385** as a colorless oil. The relative stereochemistry of this compound was not determined. Data for Compound **385**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.61 (d, *J* = 7.8, 1 H), 7.44 (d, *J* = 8.3Hz, 1 H), 7.14 (t, *J* = 7.8, 1 H), 6.98 (t, *J* = 7.8, 1 H), 6.94 (d, *J* = 7.8, 1 H), 6.53 (d, *J* = 8.3, 1 H), 5.53 (dd, *J* = 10.3, 3.5, 1 H), 3.42 (bs, 1 H), 2.94 (q, *J* = 7.0, 1 H), 2.65 (s, 1 H), 1.88-1.63 (m, 2 H), 1.53-1.22 (m, 10 H), 1.44 (d, *J* = 7.0, 3 H), 1.33 (s, 3 H), 1.08 (s, 3 H), 0.94 (t, *J* = 7.2, 3 H), 0.87 (t, *J* = 7.2, 3 H).

EXAMPLE 286

(*R/S*)-5-Butyl-1,2,3,4-tetrahydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]-3-quinolinone (Compound 386, structure 10A or 11A of Scheme XXXII, where R^1=R^2=H, R^3=*n*-butyl)

To a solution of (*R/S*)-1-*t*-butoxycarbonyl-1,2,3,4-tetrahydro-2,2,4-trimethylcoumarino[3,4-*f*]-3-quinolinone (structure 6A of **Scheme XXX**, where R^1=R^2=H, an intermediate from EXAMPLE 284) (4 mg, 0.012 mmol) in THF (1 mL) at -78 °C was added 1.6M *n*-BuLi hexane solution (0.016 mL, 0.024 mmol) and the resulting mixture was warmed up slowly to -20 °C, then was quenched with water (0.5 mL). Removal of solvent provided the crude product, which was treated with TFA (0.05 mL, 0.65 mmol) and Et_3SiH (0.1 mL, 0.65 mmol) in dichloromethane (1 mL) for 60 min. The reaction was quenched with 2% NaOH (2 mL) and was extracted with EtOAc (2 x 5 mL). Removal of solvent and chromatography of the residue afforded 0.7 mg (17%) of Compound **386** as a colorless oil. The relative stereochemistry of Compound **386** was not determined. Data for Compound **386**: **^{1}H**

NMR (400 MHz, $CDCl_3$) 7.63 (d, *J* = 7.7, 1 H), 7.51 (d, *J* = 8.2, 1 H), 7.16 (t, *J* = 7.7, 1 H), 7.01 (t, *J* = 7.7, 1 H), 6.96 (d, *J* = 7.7, 1 H), 6.74 (d, *J* = 8.2, 1 H), 5.32 (dd, *J* = 10.1 and 1.0, 1 H), 3.66 (q, *J* = 7.2, 1 H), 1.98-1.90 (m, 1 H), 1.58-1.18 (m, 5 H), 1.48 (s, 3 H), 1.44 (d, *J* = 7.2, 3 H), 1.20 (s, 3 H), 0.89 (t, *J* = 7.3, 3 H).

EXAMPLE 287

(*R/S-4l,5l*)-1,2,3,4-Tetrahydro-2,2,4-trimethyl-5-phenyl-5*H*-chromeno[3,4-*f*]-3-quinolinone (Compound 387, structure **18A** of **Scheme XXXIII**, where R^1=R^2=H, R^3=phenyl) This compound, along with Compound **388** (EXAMPLE 288), was prepared by the same Boc-protection/hydroboration/oxidation/deprotection procedure as described in the synthesis of Compound **234** (EXAMPLE 134) from Compound **161** (EXAMPLE 61) (40 mg, 0.11 mmol). Compound **387** (4.0 mg, 10%) was obtained as a colorless oil. Data for Compound **387**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.59 (d, *J* = 8.3, 1 H), 7.57 (d, *J* = 7.6, 1 H), 7.21-7.12 (m, 5 H), 7.05 (t, *J* = 7.6, 1 H), 6.92 (t, *J* = 7.6, 1 H), 6.86 (d, *J* = 7.6, 1 H), 6.83 (d, *J* = 8.3, 1 H), 6.37 (s, 1 H), 3.72 (bs, 1 H), 3.41 (q, *J* = 7.5, 1 H), 1.50 (d, *J* = 7.5, 3 H), 1.45 (s, 3 H), 1.17 (s, 3 H).

EXAMPLE 288

(*R/S-4l,5u*)-1,2,3,4-Tetrahydro-2,2,4-trimethyl-5-phenyl-5*H*-chromeno[3,4-*f*]-3-quinolinone (Compound **388**, structure **17A** of **Scheme XXXIII**, where R^1=R^2=H, R^3=phenyl) This compound, along with Compound **387** (EXAMPLE 287), was prepared by the same Boc-protection/hydroboration/oxidation/deprotection procedure as described in the synthesis of Compound **234** (EXAMPLE 134) from Compound **161** (EXAMPLE 61) (40 mg, 0.11 mmol). Compound **388** (7.3 mg, 18%) was obtained as a white poweder. Data for Compound **388**: mp 108-110 ^oC; **IR** (neat) 3358, 2972, 1720, 1473, 1292, 1213, 752; **^{1}H NMR** (400 MHz, $CDCl_3$) 7.66 (d, *J* = 7.7, 1 H), 7.64 (d, *J* = 8.2, 1 H), 7.20 (s, 5 H), 7.06 (t, *J* = 7.7, 1 H), 6.95 (t, *J* = 7.7, 1 H), 6.83 (d, *J* = 8.2, 1 H), 6.77 (d, *J* = 7.7, 1 H), 6.39 (s, 1 H), 3.72 (bs, 1 H), 3.58 (q, *J* = 7.4, 1 H), 1.44 (s, 3 H), 1.23 (s, 3 H), 0.80 (d, *J* = 7.4, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$) 214.4, 151.0, 143.2, 139.3, 131.1, 128.9, 128.8, 128.6, 128.5, 123.4, 122.7, 122.2, 122.1, 122.0, 118.3, 116.6, 75.4, 60.2, 43.9, 28.1, 27.3, 16.3. Anal. ($C_{25}H_{23}NO_2$-3/4H_2O) C, H, N.

EXAMPLE 289

(*Z*)-(*R*/*S*)-5-(3-Fluorobenzylidene)-1,2,3,4-tetrahydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]-3-quinolinone (Compound **389**, structure **19A** of **Scheme XXXIV**, where R^1=R^2=H, R^3=3-fluorophenyl)

To a solution of (*R*/*S*)-1-*t*-butoxycarbonyl-1,2,3,4-tetrahydro-2,2,4-trimethylcoumarino[3,4-*f*]-3-quinolinone (structure 6A of **Scheme XXX**, where R^1=R^2=H, an intermediate from EXAMPLE 284) (10 mg, 0.025 mmol) in THF (1 mL) at -78 °C was added freshly prepared 1.0 M 3-fluorobenzylmagnesium bromide (0.06 mL, 0.06 mmol) and the reaction was slowly warmed up to rt and was quenched with water (1 mL). The mixture was extracted with EtOAc (2 x 5 mL) and was concentrated to provide the crude intermediate, which was treated with excess TFA (0.2 mL) in dichloromethane (1 mL) for 30 min and then quenched with 5 % NaOH (5 mL). The mixture was extracted with EtOAc (2 x 10 mL), concentrated and chromatographied to afford 6.0 mg (60%) of Compound **389** as a yellowish oil. Data for Compound **389**: **IR** (neat) 3356, 1716, 1604, 1469, 1251; **^{1}H NMR** (400 MHz, $CDCl_3$) 7.73 (d, *J* = 7.8, 1 H), 7.70 (d, *J* = 11.1, 1 H), 7.60 (d, *J* = 8.3, 1 H), 7.42 (d, *J* = 7.8, 1 H), 7.31 (td, *J* = 8.0 and 6.2, 1 H), 7.22 (d, *J* = 8.1, 1 H), 7.18 (d, *J* = 7.0, 1 H), 7.08 (t, *J* = 7.1, 1 H), 6.94 (td, *J* = 8.4 and 2.4, 1 H), 6.85 (d, *J* = 8.3, 1 H), 5.87 (s, 1 H), 4.33 (q, *J* = 7.3, 1 H), 3.78 (s, 1 H), 1.56 (d, *J* = 7.3, 3 H), 1.51 (s, 3 H), 1.24 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$) 2.14.0, 162.4 (d, *J* = 244.0 Hz), 152.3, 147.0, 144.2, 137.2 (d, *J* = 8.1 Hz), 129.8 (d, *J* = 8.8 Hz), 128.7, 128.0, 125.4, 124.2, 123.0, 122.6, 122.4, 121.9, 121.8, 118.1, 116.5, 115.8 (d, *J* = 23.1 Hz), 114.1, 113.8 (d, *J* = 21.1 Hz), 60.1, 44.9, 27.7, 27.2, 17.4. A minor 1.0 mg (<10%) product was also isolated and identified as (*E*)-(*R*/*S*)-5-(3-fluorobenzylidene)-1,2,3,4-tetrahydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]-3-quinolinone; **^{1}H NMR** (400 MHz, $CDCl_3$) 7.78 (d, *J* = 7.9, 1 H), 7.70 (d, *J* = 8.7, 1 H), 7.67 (d, *J* = 10.2, 1 H), 7.42 (d, *J* = 7.8, 1 H), 7.35-7.26 (m, 3 H), 7.21 (d, *J* = 8.1, 1 H), 7.10 (t, *J* = 8.2, 1 H), 6.97 (td, *J* = 8.4 and 2.4, 1 H), 5.80 (s, 1 H), 4.28 (q, *J* = 7.3, 1 H), 3.55 (bs, 1 H), 1.88 (s, 3 H), 1.76 (d, *J* = 7.3, 3 H), 1.33 (s, 3 H).

EXAMPLE 290

(*R/S-4l,6u*)-1,2,3,4-Tetrahydro-2,2,4-trimethyl-6-phenyl-5*H*-isochromeno[3,4-*f*]-3-quinolinone (Compound **390**, structure **23A** of **Scheme XXXV**, where R^1=phenyl))

1,2-Dihydro-2,2,4-trimethyl-10-isocoumarino[3,4-*f*]quinoline (Compound **21A**, **Scheme XXXV**) This compound was prepared by General Method 8 (EXAMPLE 138) from 7-amino-3,4-benzocoumarin to afford 1,2-dihydro-2,2,4-trimethyl-10-isocoumarino[3,4-*f*]quinoline (150 mg, 0.52 mmol, 60%) as a yellow solid. Data for 1,2-dihydro-2,2,4-trimethyl-10-isocoumarino[3,4-*f*]quinoline: mp 197-199 °C; **IR** (KBr) 3350, 2960, 1711, 1608, 1566, 1468 and 1311; **^{1}H NMR** (400 MHz, $CDCl_3$) 8.20 (d, *J* = 7.6, 1 H), 8.10 (d, *J* = 7.6, 1 H), 7.83 (d, *J* = 8.6, 1 H), 7.77 (t, *J* = 7.6, 1 H), 7.44 (t, *J* = 7.6, 1 H), 6.64 (d, *J* = 8.6, 1 H), 5.88 (bs, 1 H), 5.38 (s, 1 H), 2.39 (s, 3 H), 1.29 (s, 6 H); **^{13}C NMR** (100 MHz, $CDCl_3$) 161.5, 149.6, 146.9, 136.6, 134.8, 130.4, 128.3, 126.6, 122.8, 120.8, 119.0, 111.1, 109.6, 108.6, 51.7, 30.4, 23.6.

1,2-Dihydro-2,2,4-trimethyl-6-phenyl-5*H*-isochromeno[3,4-*f*]quinoline (structure **22A** of **Scheme XXXV**, where R^1=phenyl) This compound was prepared by General Method 5 (EXAMPLE 60) from 1,2-dihydro-2,2,4-trimethyl-10-isocoumarino[3,4-*f*]quinoline (60 mg, 0.20 mmol) and bromobenzene (157 mg, 1.0 mmol) to afford 60 mg (85%) as a colorless oil. Data for 1,2-dihydro-2,2,4-trimethyl-6-phenyl-5*H*-isochromeno[3,4-*f*]quinoline: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.60 (d, *J* = 7.7, 1 H), 7.44 (d, *J* = 8.3, 1 H), 7.43-7.30 (m, 7 H), 7.10 (t, *J* = 7.7, 1 H), 6.73 (d, *J* = 7.7, 1 H), 6.04 (s, 1 H), 5.22 (s, 1 H), 3.87 (bs, 1 H), 2.11 (s, 3 H), 1.26 (s, 3 H), 1.23 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$) 152.0, 146.3, 145.2, 139.6, 132.9, 131.6, 129.3, 128.6, 128.4, 125.9, 125.6, 123.5, 121.2, 113.9, 111.2, 108.5, 80.1, 51.4, 30.3, 30.1, 23.5.

(*R/S-4l,6u*)-1,2,3,4-Tetrahydro-2,2,4-trimethyl-6-phenyl-5*H*-isochromeno[3,4-*f*]-3-quinolinone This compound was prepared by the same Boc-protection/hydroboration/oxidation/deprotection procedure as described in the synthesis of Compound **234** (EXAMPLE 134) from 1,2-dihydro-2,2,4-trimethyl-6-phenyl-5*H*-isochromeno[3,4-*f*]quinoline (30 mg, 0.085 mmol). Compound **390** (2.2 mg, 7%) was obtained as a colorless oil, along with xx mg (14%) of Compound **391** (EXAMPLE 291).

Data for Compound **390**: **^{1}H NMR** (400 MHz, CDCl$_3$) 7.65 (d, *J* = 7.8, 1 H), 7.49 (d, *J* = 8.4, 1 H), 7.37 (t, *J* = 7.8, 1 H), 7.30 (s, 5 H), 7.19 (t, *J* = 7.8, 1 H), 6.89 (d, *J* = 7.8, 1 H), 6.38 (d, *J* = 8.4, 1 H), 6.14 (s, 1 H), 3.83 (q, *J* = 7.5, 1 H), 3.67 (bs, 1 H), 1.41 (s, 3 H), 1.39 (d, *J* = 7.5, 3 H), 1.12 (s, 3 H).

EXAMPLE 291

(*R/S-4l,6l*)-1,2,3,4-Tetrahydro-2,2,4-trimethyl-6-phenyl-5H-isochromeno[3,4-*f*]-3-quinolinone (Compound **391**, structure **24A** of **Scheme XXXV**, where R^{1}=phenyl)

Compound **391** (4.4 mg, 14%) was obtained as a colorless oil along with Compound **390** as described above (EXAMPLE 290). Data for Compound **391**: **IR** (neat) 3358, 1716, 1614, 1471, 1439, 1030; **^{1}H NMR** (400 MHz, CDCl$_3$) 7.66 (d, *J* = 7.7, 1 H), 7.53 (d, *J* = 8.3, 1 H), 7.35 (s, 5 H), 7.34 (t, *J* = 7.7, 1 H), 7.15 (t, *J* = 7.7, 1 H), 6.79 (d, *J* = 7.7, 1 H), 6.12 (s, 1 H), 3.82 (q, *J* = 7.3, 1 H), 3.66 (bs, 1 H), 1.41 (s, 3 H), 1.23 (s, 3 H), 1.14 (d, *J* = 7.3, 3 H).

EXAMPLE 292

(*Z*)-(*R/S*)-5-(Benzylidene)-1,2,3,4-tetrahydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]-3-quinolinone (Compound **392**, structure **19A** of **Scheme XXXIV**, where R^{1}=R^{2}=H, R^{3}=phenyl)

To a solution of (*R/S*)-1-*t*-butoxycarbonyl-1,2,3,4-tetrahydro-2,2,4-trimethylcoumarino[3,4-*f*]-3-quinolinone (structure 6A of **Scheme XXX**, where R^{1}=R^{2}=H, an intermediate from EXAMPLE 284) (10 mg, 0.025 mmol) in THF (1 mL) at -78 °C was added 1.0 M benzylmagnesium bromide (0.06 mL, 0.06 mmol) and the reaction was slowly warmed up to rt and was quenched with water (1 mL). The mixture was extracted with EtOAc (2 x 5 mL) and was concentrated to provide the crude intermediate, which was treated with excess TFA (0.2 mL) in dichloromethane (1 mL) for 30 min and then quenched with 5 % NaOH (5 mL). The mixture was extracted with EtOAc (2 x 10 mL), concentrated and chromatographied to afford 3.8 mg (40%) of Compound **392** as a colorless oil. Data for Compound **392**: **IR** (neat) 3354, 1716, 1469, 1261, 1045; **^{1}H NMR** (400 MHz, CDCl$_3$) 7.81 (d, *J* = 7.3, 2 H), 7.72 (d, *J* = 7.7, 1 H), 7.59 (d, *J* = 8.4, 1 H), 7.39 (t, *J* = 7.3, 2 H), 7.24-7.18 (m, 2 H), 7.17 (d, *J* = 7.7, 1 H), 7.08 (t, *J* = 7.7, 1 H), 6.83 (d, *J* = 8.4, 1 H), 5.91 (s, 1 H), 4.37 (q, *J* = 7.3, 1 H), 3.76 (s, 1 H), 1.57 (d, *J* = 7.3, 3 H), 1.51 (s, 3 H), 1.24 (s, 3 H); **^{13}C NMR** (100 MHz, CDCl$_3$) 214.1, 152.7, 146.0, 144.2, 135.1, 129.5, 128.6, 128.5, 127.1, 124.2, 122.8, 122.4, 122.2, 121.8, 121.7, 117.8, 116.5, 115.4, 60.1, 44.9, 27.7, 27.2, 17.4.

EXAMPLE 293

(*R/S-4l,5u*)-5-(3-Fluorophenyl)-1,2,3,4-tetrahydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]-3-quinolinone (Compound 393, structure **17A** of **Scheme XXXIII**, where R^1=R^2=H, R^3=3-fluorophenyl)

This compound, along with Compound **394** (EXAMPLE 294), was prepared by the same Boc-protection/hydroboration/oxidation/deprotection procedure as described in the synthesis of Compound **234** (EXAMPLE 134) from Compound **191** (EXAMPLE 91) (30 mg, 0.081 mmol). Compound **393** (6.9 mg, 22%) was obtained as a colorless oil. Data for Compound **393**: **IR** (neat) 3356, 1719, 1602, 1487, 1288, 1209, 1028; ^{1}**H NMR** (400 MHz, CDCl$_3$) 7.66 (d, *J* = 7.7, 1 H), 7.64 (d, *J* = 8.3, 1 H), 7.19 (td, *J* = 7.9, 5.8, 1 H), 7.09-6.86 (m, 5 H), 6.85 (d, *J* = 8.3, 1 H), 6.78 (d, *J* = 7.7, 1 H), 6.38 (s, 1 H), 3.72 (bs, 1 H), 3.58 (q, *J* = 7.4, 1 H), 1.44 (s, 3 H), 1.23 (s, 3 H), 0.87 (d, *J* = 7.4, 3 H); ^{13}**C NMR** (100 MHz, CDCl$_3$) 214.1, 162.9 (d, *J* = 246.2), 150.7, 143.3, 141.8 (d, *J* = 6.3), 130.4, 130.2, 130.1, 128.6, 124.6, 123.3, 122.7, 122.4, 122.3 (d, *J* = 22.1), 118.3, 116.9, 115.8 (d, *J* = 21.4), 74.5, 60.2, 43.9, 28.1, 27.3, 14.4.

EXAMPLE 294

(*R/S-4l,5l*)-5-(3-Fluorophenyl)-1,2,3,4-tetrahydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]-3-quinolinone (Compound 394, structure **18A** of **Scheme XXXIII**, where R^1=R^2=H, R^3=3-fluorophenyl)

This compound, along with Compound **393** (EXAMPLE 293), was prepared by the same Boc-protection/hydroboration/oxidation/deprotection procedure as described in the synthesis of Compound **234** (EXAMPLE 134) from Compound **191** (EXAMPLE 91) (30 mg, 0.081 mmol). Compound **394** (5.0 mg, 16%) was obtained as a colorless oil. Data for Compound **394**: **IR** (neat) 3356, 1719, 1608, 1473, 1288, 1209, 1039; ^{1}**H NMR** (400 MHz, CDCl$_3$) 7.60 (d, *J* = 8.3, 1 H), 7.58 (d, *J* = 7.7, 1 H), 7.15 (td, *J* = 7.9, 5.8, 1 H), 7.09 (t, *J* = 7.7, 1 H), 6.97-80 (m, 6 H), 6.34 (s, 1 H), 3.73 (s, 1 H), 3.38 (q, *J* = 7.3, 1 H), 1.50 (d, *J* = 7.3, 3 H), 1.46 (s, 3 H), 1.19 (s, 3 H); ^{13}**C NMR** (100 MHz, CDCl$_3$) 213.2, 162.9 (d, *J* = 247), 150.8, 142.7, 141.6 (d, *J* = 6.4), 130.2, 130.1, 129.9, 128.5, 123.6, 122.8, 122.7, 122.4, 122.2, 118.3, 116.8, 115.5 (d, *J* = 21.6), 114.9 (d, *J* = 22.6 Hz), 74.2, 60.1, 43.0, 27.3, 26.6, 18.4.

EXAMPLE 295

(*R/S-4l,5l*)-1,2,3,4-Tetrahydro-2,2,4-trimethyl-5-[3-(trifluoromethyl)phenyl]-5*H*-chromeno[3,4-*f*]-3-quinolinone (Compound **395**, structure **18A** of Scheme **XXXIII**, where R^1=R^2=H, R^3=3-(trifluoromethyl)phenyl)

This compound, along with Compound **396** (EXAMPLE 396), was prepared by the same Boc-protection/hydroboration/oxidation/deprotection procedure as described in the synthesis of Compound **234** (EXAMPLE 134) from Compound **195** (EXAMPLE 95) (20 mg, 0.049 mmol). Compound **395** (3.2 mg, 15%) was obtained as a colorless oil. Data for Compound **395**: **IR** (neat) 3354, 2926, 1720, 1607, 1473, 1211, 1126, 1074; **^{1}H NMR** (400 MHz, $CDCl_3$) 7.61 (d, *J* = 8.3, 1 H), 7.57 (d, *J* = 7.7, 1 H), 7.42 (t, *J* = 7.7, 1 H), 7.39 (s, 1 H), 7.38-7.30 (m, 2 H), 7.09 (t, *J* = 7.7, 1 H), 6.95 (d, *J* = 7.7, 1 H), 6.91 (d, *J* = 8.4, 1 H), 6.86 (d, *J* = 8.3, 1 H), 6.39 (s, 1 H), 3.77 (s, 1 H), 3.37 (q, *J* = 7.3, 1 H), 1.50 (d, *J* = 7.3, 3 H), 1.48 (s, 3 H), 1.20 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$) 213.1, 150.7, 142.8, 131.1, 129.4, 129.1, 128.6, 125.4, 124.6, 123.0, 122.7, 122.6, 122.5, 122.2, 118.3, 117.0, 74.0, 60.2, 43.1, 27.1, 26.5, 18.4.

EXAMPLE 296

(*R/S-4l,5u*)-1,2,3,4-Tetrahydro-2,2,4-trimethyl-5-[3-(trifluoromethyl)phenyl]-5*H*-chromeno[3,4-*f*]-3-quinolinone (Compound **396**, structure **17A** of Scheme **XXXIII**, where R^1=R^2=H, R^3=3-(trifluoromethyl)phenyl)

This compound, along with Compound **395** (EXAMPLE 395), was prepared by the same Boc-protection/hydroboration/oxidation/deprotection procedure as described in the synthesis of Compound **234** (EXAMPLE 134) from Compound **195** (EXAMPLE 95) (20 mg, 0.049 mmol). Compound **396** (3.2 mg, 15%) was obtained as a colorless oil. Data for Compound **396**: **IR** (neat) 3356, 2928, 1718, 1602, 1330, 1126, 1074; **^{1}H NMR** (400 MHz, $CDCl_3$) 7.67 (d, *J* = 8.3, 1 H), 7.65 (d, *J* = 7.7, 1 H), 7.52 (s, 1 H), 7.48 (m, 1 H), 7.35-7.30 (m, 2 H), 7.08 (t, *J* = 7.7, 1 H), 6.98 (t, *J* = 7.7, 1 H), 6.88 (d, *J* = 8.3, 1 H), 6.78 (d, *J* = 7.7, 1 H), 6.43

(s, 1 H), 3.75 (s, 1 H), 3.57 (q, *J* = 7.4, 1 H), 1.45 (s, 3 H), 1.24 (s, 3 H), 0.86 (d, *J* = 7.4, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$) 214.0, 150.5, 143.3, 140.3, 132.1, 131.2 (q, *J* = 31.7), 130.0, 129.1, 128.7, 125.7, 123.3, 122.7, 122.6, 122.5, 122.2, 118.3, 117.1, 74.3, 60.2, 43.8, 28.2, 27.3, 16.5.

EXAMPLE 297

(*R*/*S*-*3l*,*4u*,*5u*)-5-(4-Chlorophenyl)-1,2,3,4-tetrahydro-3-methoxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **397**, structure **26A** of **Scheme XXXVI**, where R^1=R^2=H, R^3=4-chlorophenyl, R^4=methyl)

To a solution of (*R*/*S*-*3l*,*4u*,*5u*)-5-(4-chlorophenyl)-1,2,3,4-tetrahydro-3-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (structure 14A of **Scheme XXXIII**, where R^1=R^2=H, R^3=4-chlorophenyl, an intermediate from EXAMPLE 135) (8 mg, 0.016 mmol) in DMF (0.5 mL) and excess MeI (0.5 mL) was added 60% NaH in mineral oil (10 mg, 0.25 mmol). The resulting white slurry was stirred at rt for 2 h and was quenched with water (5 mL). The mixture was extracted with EtOAc (2 x 10 mL) and was concentrated to give the crude product, which was treated with TFA (0.2 mL) in CH_2Cl_2 (1 mL) for 60 min and was quenched with 5 % NaOH (5 mL). The mixture was extracted with EtOAc (2 x 10 mL), concentrated and was purified by silica gel chromatography to afford 5.0 mg (75%) of Compound **397** as a colorless oil. Data for Compound **397**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.53 (d, *J* = 7.7, 1 H), 7.48 (d, *J* = 8.4, 1 H), 7.12 (s, 4 H), 7.04 (t, *J* = 7.7, 1 H), 6.89 (t, *J* = 7.7, 1 H), 6.87 (d, *J* = 7.7, 1 H), 6.63 (d, *J* = 8.4, 1 H), 6.48 (s, 1 H), 3.74 (bs, 1 H), 3.26 (s, 3 H), 3.08 (d, *J* = 3.8, 1 H), 2.83 (qd, *J* = 7.3, 3.8, 1 H), 1.52 (d, *J* = 7.3, 3 H), 1.35 (s, 3 H), 1.50 (s, 3 H).

EXAMPLE 298

(*R*/*S*-*3l*,*4u*,*5l*)-5-(4-Chlorophenyl)-1,2,3,4-tetrahydro-3-methoxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **398**, structure **25A** of **Scheme XXXVI**, where R^1=R^2=H, R^3=4-chlorophenyl, R^4=methyl)

To a solution of (*R*/*S*-*3l*,*4u*,*5l*)-5-(4-chlorophenyl)-1,2,3,4-tetrahydro-3-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (structure 13A of **Scheme XXXIII**, where R^1=R^2=H, R^3=4-chlorophenyl, an intermediate from EXAMPLE 135) (8 mg, 0.016 mmol) in DMF (0.5 mL) and excess MeI (0.5 mL) was added 60% NaH in mineral oil (10 mg, 0.25

mmol). The resulting white slurry was stirred at rt for 2 h and was quenched with water (5 mL). The mixture was extracted with EtOAc (2 x 10 mL) and was concentrated to give the crude product, which was treated with TFA (0.2 mL) in CH_2Cl_2 (1 mL) for 60 min and was quenched with 5 % NaOH (5 mL). The mixture was extracted with EtOAc (2 x 10 mL), concentrated and was purified by silica gel chromatography to afford 4.7 mg (70%) of Compound **398** as a colorless oil. Data for Compound **398**: ^{1}H NMR (400 MHz, $CDCl_3$) 7.55 (d, J = 7.7, 1 H), 7.47 (d, J = 8.4, 1 H), 7.16 (d, J = 8.7, 2 H), 7.12 (d, J = 8.7, 2 H), 6.97 (t, J = 7.7, 1 H), 6.89 (t, J = 7.7, 1 H), 6.73 (d, J = 7.7, 1 H), 6.68 (d, J = 8.4, 1 H), 6.34 (s, 1 H), 3.65 (bs, 1 H), 3.53 (s, 3 H), 3.03 (s, 1 H), 3.02 (qd, J = 7.0, 0.8, 1 H), 1.30 (s, 3 H), 1.11 (s, 3 H), 0.88 (d, J = 7.0, 3 H).

EXAMPLE 299

(*R/S-3l,4u,5l*)-5-(4-Chlorophenyl)-1,2,3,4-tetrahydro-3-propyloxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **399**, structure **25A** of **Scheme XXXVI**, where R^1=R^2=H, R^3=4-chlorophenyl, R^4=propyl)

To a solution of (*R/S-3l,4u,5l*)-5-(4-chlorophenyl)-1,2,3,4-tetrahydro-3-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (structure 13A of **Scheme XXXIII**, where R^1=R^2=H, R^3=4-chlorophenyl, an intermediate from EXAMPLE 135) (7 mg, 0.014 mmol) in DMF (0.5 mL) and excess PrI (0.5 mL) was added 60% NaH in mineral oil (10 mg, 0.25 mmol). The resulting white slurry was stirred at rt for 2 h and was quenched with water (5 mL). The mixture was extracted with EtOAc (2 x 10 mL) and was concentrated to give the crude product, which was treated with TFA (0.2 mL) in CH_2Cl_2 (1 mL) for 60 min and was quenched with 5 % NaOH (5 mL). The mixture was extracted with EtOAc (2 x 10 mL), concentrated and was purified by silica gel chromatography to afford 2.5 mg (40%) of Compound **399** as a colorless oil. Data for Compound **399**: ^{1}H NMR (400 MHz, $CDCl_3$) 7.57 (d, J = 7.7, 1 H), 7.48 (d, J = 8.4, 1 H), 7.16 (d, J = 8.6, 2 H), 7.12 (d, J = 8.6, 2 H), 6.99 (t, J = 7.7, 1 H), 6.89 (t, J = 7.7, 1 H), 6.73 (d, J = 7.7, 1 H), 6.68 (d, J = 8.4, 1 H), 6.33 (s, 1 H), 3.65 (bs, 1 H), 3.58 (m, 2 H), 3.11 (d, J = 5.8, 1 H), 3.00 (qd, J = 7.0, 5.8, 1 H), 1.65-1.50 (m, 2 H), 1.30 (s, 3 H), 1.10 (s, 3 H), 0.93 (t, J = 7.4, 3 H), 0.88 (d, J = 7.0, 3 H).

EXAMPLE 300

(*R/S-3l,4u,5u*)-5-(4-Chlorophenyl)-1,2,3,4-tetrahydro-3-propyloxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **400**, structure **26A** of **Scheme XXXVI**, where R^1=R^2=H, R^3=4-chlorophenyl, R^4=propyl)

To a solution of (*R/S-3l,4u,5u*)-5-(4-chlorophenyl)-1,2,3,4-tetrahydro-3-hydroxy-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (structure 14A of **Scheme XXXIII**, where R^1=R^2=H, R^3=4-chlorophenyl, an intermediate from EXAMPLE 135) (8 mg, 0.016 mmol) in DMF (0.5 mL) and excess PrI (0.5 mL) was added 60% NaH in mineral oil (10 mg, 0.25 mmol). The resulting white slurry was stirred at rt for 2 h and was quenched with water (5 mL). The mixture was extracted with EtOAc (2 x 10 mL) and was concentrated to give the crude product, which was treated with TFA (0.2 mL) in CH_2Cl_2 (1 mL) for 60 min and was quenched with 5 % NaOH (5 mL). The mixture was extracted with EtOAc (2 x 10 mL), concentrated and was purified by silica gel chromatography to afford 2.5 mg (40%) of Compound **400** as a colorless oil. Data for Compound **400**: ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.54 (d, *J* = 7.7, 1 H), 7.48 (d, *J* = 8.4, 1 H), 7.12 (d, *J* = 8.6, 2 H), 7.09 (d, *J* = 8.6, 2 H), 7.02 (t, *J* = 7.7, 1 H), 6.89 (t, *J* = 7.7, 1 H), 6.87 (d, *J* = 7.7, 1 H), 6.62 (d, *J* = 8.4, 1 H), 6.48 (s, 1 H), 3.72 (bs, 1 H), 3.28 (m, 2 H), 3.16 (d, *J* = 4.0, 1 H), 2.78 (qd, *J* = 7.2, 4.0, 1 H), 1.51 (d, *J* = 7.2, 3 H), 1.51-1.36 (m, 2 H), 1.34 (s, 3 H), 1.14 (s, 3 H), 0.80 (t, *J* = 7.4, 3 H).

EXAMPLE 301

(*R/S-4l,5l*)-3-Benzenzylidene-5-(4-chlorophenyl)-1,2,3,4-tetrahydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]quinoline (Compound **401**, structure **27A** of **Scheme XXXVII**, where R^1=R^2=H, R^3=4-chlorophenyl, R^4=phenyl)

To a solution of Compound **234** (EXAMPLE 134) (35 mg, 0.086 mmol) in THF (4 mL) was added a 1.0M ether solution of benzylmagnesium chloride (0.3 mL, 0.3 mmol) and the reaction was stirred at rt for 2 h. The reaction mixture was quenched with water (5 mL) and extracted with EtOAc (2 x 10 mL). Removal of solvent and chromatography of the crude residue afforded the adduct in 66% yield as a 8:1 mixture of two isomers. The adduct intermediate (8 mg, 0.016 mmol) and Burgess reagent (15 mg, 0.063 mmol) in benzene were heated at reflux for 2 h. Removal of solvent and purification of the mixture on a prep TLC plate using a 25% mixture of EtOAc/Hexane as solvent afforded 0.5 mg (7%) of

Compound **401** as a colorless oil. Data for Compound **401**: **^{1}H NMR** (400 MHz, $CDCl_3$) 7.61 (d, *J* = 7.7, 1 H), 7.56 (d, *J* = 8.4, 1 H), 7.43 (t, *J* = 7.5, 2 H), 7.32 (t, *J* = 7.7, 1 H), 7.21 (d, *J* = 7.6, 2 H), 7.16 (d, *J* = 8.6, 2 H), 7.05-6.93 (m, 2 H), 6.96 (d, *J* = 8.6, 2 H), 6.72 (d, *J* = 8.4, 1 H), 6.68 (d, *J* = 7.7, 1 H), 6.38 (s, 1 H), 6.05 (s, 1 H), 4.02 (q, *J* = 7.5, 1 H), 3.55 (bs, 1 H), 1.52 (s, 3 H), 1.41 (s, 3 H), 0.84 (d, *J* = 7.5, 3 H).

EXAMPLE 302

(*R/S-4l,5u*)-5-(4-Chlorophenyl)-1,2,3,4-tetrahydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]-3-quinolinone (Compound **402**, structure **53** of **Scheme XV**, where R^1=H, R^2=fluoro, R=4-chlorophenyl)

This compound (2.2 mg, 4%) was prepared in a manner similar to that described for the preparation of Compound **234** (EXAMPLE 134) from Compound **214** (EXAMPLE 114) (50 mg, 0.16 mmol). In addition, 2.2 mg (4%) of Compound **403** (EXAMPLE 303) was also obtained as a clear-colorless oil. Data for compound **402**: Rf=0.38 (silica gel, 25% EtOAc:hex); **^{1}H NMR** (400 MHz, $CDCl_3$) 7.51 (d, *J* = 8.5, 1 H), 7.23 (d, *J* = 8.5, 1 H), 7.16 (d, *J* = 8.5, 2 H), 7.04 (d, *J* = 8.5, 2 H), 6.84 (d, *J* = 8.5, 1 H), 6.78 (m, 2 H), 6.30 (s, 1 H), 3.79 (brs, 1 H), 3.33 (q, *J* = 7.5, *J* = 7.5, 1 H), 1.49 (d, *J* = 7.5, 3 H), 1.46 (s, 3 H), 1.25 (s, 3H).

EXAMPLE 303

(*R/S-4l,5l*)-5-(4-Chlorophenyl)-1,2,3,4-tetrahydro-2,2,4-trimethyl-5*H*-chromeno[3,4-*f*]-3-quinolinone (Compound **403**, structure **52** of **Scheme XV**, where R^1=H, R^2=fluoro, R=4-chlorophenyl)

This compound (2.2 mg, 4%) was obtained along with Compound **402** as described above (EXAMPLE 302). Data for compound **403**: Rf=0.38 (silica gel, 25% EtOAc:hex); **^{1}HNMR** (400 MHz, $CDCl_3$) 7.56 (d, *J* = 8.5, 1 H), 7.31 (d, *J* = 8.5, 1 H), 7.20 (d, *J* = 8.5, 2 H), 7.10 (d, *J* = 8.5, 2 H), 6.85 (d, *J* = 8.5, 1 H), 6.74 (m, 2 H), 6.35 (s, 1 H), 3.79 (brs, 1 H), 3.55 (q, *J* = 7.5, *J* = 7.5, 1 H), 1.45 (s, 3 H), 1.26 (s, 3 H), 0.86 (d, *J* = 7.5, 3 H).

EXAMPLE 304

(*R/S*)-1,2,3,4-Tetrahydro-1,2,2,4-tetramethyl-6-trifluoromethyl-8-pyranono[5,6-*g*]quinoline (Compound **404**, structure **28A** of Scheme **XXXVIII**, where R^1=R^2=R^5=H, R^3=trifluoromethyl, Z=O)

In a flame dried r.b. flask was dissolved Compound **250** (EXAMPLE 150) (50 mg, 161 μmol) in glacial acetic acid (10 mL). To the stirred solution was added *para*-formadehyde (51 mg, 1.61 mmol, 10 equiv). The cloudy yellow solution stirred for 10 min, then $NaCNBH_3$ (50 mg, 805 μmol, 5 equiv) was added at once. Upon addition the solution emitted gas for approx. 5 min then turned a brilliant fluorescent yellow/green. After stirring at rt under a blanket of N_2 for 20 h, the solution was slowly poured over ice and quenched with NaOH (20%), extracted with EtOAc (2 x 50 mL), washed with brine (2 x 25 mL), dried over Na_2SO_4 and concentrated *in vacuo* to give 51.3 mg (99 %) of Compound **404** as a yellow-green solid. Data for Compound **404**: R_f = 0.39 (hexanes/EtOAc; 3:1). **^{1}H NMR** (400 MHz, $CDCl_3$) 7.31 (dd, *J* = 1.5, 1.5, 1 H), 6.44 (s, 1 H), 6.35 (s, 1 H), 2.90 (s, 3 H, N-C$\underline{H}_3$), 2.83 (m, partially obscured by Me, 1 H, C4-H), 1.84 (dd, *J* = 4.2, 13.3, 1 H, C3-H), 1.53 (dd, *J* = 13.0, 13.0, 1 H), 1.36 (d, *J* = 6.6, 3 H, C4-C$\underline{H}_3$), 1.35 (s, 3 H, C2-C$\underline{H}_3$), 1.29 (s, 3 H, C2-C$\underline{H}_3$).

EXAMPLE 305

(*R/S*)-5-(3-Furyl)-1,2,3,4-tetrahydro-2,2,4-trimethyl-8-pyranono[5,6-*g*]quinoline (Compound **405**, structure **63** of Scheme **XVIII**, where R^1=R^2=H, R3=^{3}-furyl, Z=O)

In a oven dried pressure tube equivuipped with a magnetic stir bar was dissolved (*R/S*)-1,2,3,4-tetrahydro-2,2,4-trimethyl-7-hydroxyquinoline (EXAMPLE 150) (50.8 mg, 292 μmol), ethyl 3-keto-3-(3-furyl)propionate (0.10 mL, 642 μmol, 2.2 equiv) and $ZnCl_2$ (119 mg, 876 μmol, 3 equiv) in absolute ethanol (6 mL). The solution was heated at 105°C for 19 h. The cooled solution was concentrated on Celite™ to give a free flowing powder which was purified *via* silica gel flash column chromatography using a solvent system of hexanes/ethyl acetate (4:1) to 14.6 mg (16%) of Compound **405** as a yellow oil. Data for Compound **405**: R_f = 0.26 (hexanes/EtOAc; 3:1); **^{1}H NMR** (400 MHz, $CDCl_3$) 7.76 (s, 1 H), 7.58 (dd, *J* = 1.4, 3.0, 1 H), 7.48 (s, 1 H), 6.66 (s, 1 H), 6.37 (s, 1 H), 6.06 (s, 1 H), 4.37 (br s, 1 H, NH), 2.91 (m, 1 H, C4-H), 1.78 (dd, *J* = 4.1, 13, 1 H, C3-H), 1.44 (dd, *J* = 13, 13, 1 H, C3-H), 1.33 (d, $J = 6.7$, 3 H, C4- CH_3), 1.31 (s, 3 H, C2- CH_3), 1.23 (s, 3 H, C2- CH_3).

EXAMPLE 306

5-(3-Furyl)-1,2-dihydro-1,2,2,4-tetramethyl-8-pyranono[5,6-*g*]quinoline (Compound **406**, structure **60** of Scheme **XVI**, where $R^1=R^2=R^5=H$, R^3=3-furyl, Z=O)

In a flame dried r.b. flask was dissolved Compound **264** (EXAMPLE 164) (1.1 mg, 3.58 μmol) in glacial acetic acid (3 mL). To the stirred solution was added *para*-formadehyde (1.2 mg, 36 μmol, 10 equiv). The cloudy yellow solution stirred for 10 min then $NaCNBH_3$ (1.1 mg, 17 μmol, 5 equiv) was added at once. Upon addition the solution emitted gas for approx 5 min then turned bright yellow. After stirring at rt under a blanket of N_2 for 20 h the solution was slowly poured over ice and quenched with NaOH (20%), extracted with EtOAc (2 x 10 mL), washed with brine (2 x 10 mL), dried over Na_2SO_4 and concentrated *in vacuo* to give a impure product that was further purified by preparatory plate chromatography (silica gel, 1000 μm) using a solvent system of 4:1 hexanes/EtOAc to afford 0.8 mg (70 %) of Compound **406** as a yellow-green solid. Data for Compound **406**: $R_f = 0.25$ (hexanes/EtOAc; 3:1). **^{1}H NMR** (400 MHz, $CDCl_3$) 7.77 (s, 1 H), 7.57 (d, $J = 1.7$, 1 H), 7.30 (s, 1H), 6.66 (d, $J = 1.7$, 1 H), 6.40 (s, 1 H), 6.07 (s, 1 H), 5.33 (s, 1 H, C3-H), 2.89 (s, 3 H, N-C$\underline{H}_3$), 1.95 (d, $J = 1.1$, 3 H, C4-C$\underline{H}_3$), 1.38 (s, 6 H, (C$\underline{H}_3$)$_2$).

EXAMPLE 307

5-(3-Furyl)-1,2-dihydro-1,2,2,4-tetramethyl-8-thiopyranono[5,6-*g*]quinoline (Compound **407**, structure **29A** of Scheme **XXXIX**, where $R^1=R^2=R^5=H$, R^3=3-furyl, Z=O)

In a dry r.b. flask was dissolved LG12066X (5.2 mg, 16.1 μmol) in glacial acetic acid (5 mL). To the stirred solution was added *para*-formadehyde (5.4 mg, 160 μmol, 10 equiv). The cloudy red solution stirred for 10 min then $NaCNBH_3$ (5.1 mg, 80 μmol, 5 equiv) was added at once. After stirring under a blanket of N_2 for 12 h the solution was slowly poured over ice and quenched with NaOH (20%), extracted with EtOAc (2 x 20 mL), washed with brine (2 x 20 mL), dried over Na_2SO_4 and concentrated *in vacuo* to give an impure product that was further purified by prep TLC (silica gel, 1000 μm) using a solvent system of 4:1 hexanes/EtOAc to afford 3.2 mg (60%) of Compound **407** as a red solid. Data for

Compound **407**: R_f = 0.39 (hexanes/EtOAc; 3:1). ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.21 (d, *J* = 1.7, 1 H), 7.16 (s, 1 H), 6.51 (s, 1 H), 5.42 (s, 1 H, C3-H), 2.90 (s, 3 H, N-CH$_3$), 2.00 (d, *J* = 1.1, 3 H, C4-CH$_3$), 1.41 (s, 6 H, (CH$_3$)$_2$).

EXAMPLE 308

6-Chloro-5-(3-furyl)-1,2-dihydro-1,2,2,4-tetramethyl-8-pyranono[5,6-*g*]quinoline (Compound **408**, structure **60** of **Scheme XVI**, where R^1=R^5=H, R2=chloro, R^3=trifluoromethyl, Z=O)

In a dry r.b. flask was dissolved Compound **258** (EXAMPLE 158) (5.9 mg, 17.2 µmol) in glacial acetic acid (5 mL). To the stirred solution was added *para*-formadehyde (5.5 mg, 172 µmol, 10 equiv). The cloudy yellow solution stirred for 10 min then $NaCNBH_3$ (5.8 mg, 86 µmol, 5 equiv) was added at once. After stirring under a blanket of N_2 for 12 h the solution was slowly poured over ice and quenched with NaOH (20%), extracted with EtOAc (2 x 20 mL), washed with brine (2 x 20 mL), dried over Na_2SO_4 and concentrated *in vacuo* to give an impure product that was further purified by 3 consecutive prep TLC's (silica gel, 1000 µm) using a solvent system of 4:1 hexanes/EtOAc to afford 2.5 mg (40%) of Compound **408** as a orange/yellow solid. Data for Compound **408**: R_f = 0.36 (hexanes/EtOAc; 3:1). ^{1}**H NMR** (400 MHz, CDCl3) 7.32 (d, *J* = 1.7, 1 H), 6.33 (s, 1 H), 5.38 (s, 1 H, C3-H), 2.88 (s, 3 H, N-CH3), 1,99 (d, *J* = 1.1, 3 H, C4-CH3), 1,39 (s, 6 H, (CH3)2).

EXAMPLE 309

1,2,3,4-Tetrahydro-2,2,4,10-tetramethyl-6-trifluoromethyl-8-pyridono[5,6-*g*]quinoline (Compound **409**, structure **63** of **Scheme XVIII**, where R^1=methyl, R^2=H, R^3=trifluoromethyl, Z=NH)

7-*tert*-Butyloxycarbamoyl-1,2,3,4-tetrahydro-2,2,4,8-tetramethylquinoline (structure 72 of **Scheme XVIII**, where R^1=methyl, P=*t*-butoxy, Z=NH). This compound was prepared from 7-*tert*-butyloxycarbamoyl-1,2-dihydro-2,2,4,8-tetramethylquinoline (EXAMPLE 155) (4.50 g, 14.9 mmol) according to the general hydrogenation procedure previously described (EXAMPLE 160), affording 4.48 g (99%) of the desired tetrahydroquinoline as a white solid. Data for 7-*tert*-butyloxycarbamoyl-1,2,3,4-tetrahydro-2,2,4,8-tetramethylquinoline: ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.03 (d, 1H, *J* = 8.3, 5-H), 6.81 (d, 1H, *J* = 8.2, 6-H), 6.13 (br s, 1H, BOCN*H*), 3.43 (br s, 2H, NH_2), 2.91 (ddq, 1H, *J* = 19.0, 12.8, 6.6, 4-H), 1.96 (s, 3H, 8-CH_3), 1.73 and 1.40 (d of ABq, 2H, J_{AB} = 12.8, J_A = 5.6, J_B = 12.6, 3-H), 1.31 (d, 3H, *J* = 6.7, 4-CH_3), 1.28 and 1.16 ppm [2s, 2 x 3H, 2-(CH_3)2].

7-Amino-1,2-dihydro-2,2,4,8-tetramethylquinoline. This compound was prepared by General Method 12 (EXAMPLE 147) from 7-*tert*-butyloxycarbamoyl-1,2,3,4-tetrahydro-2,2,4,8-tetramethylquinoline (4.48 g, 14.9 mmol) to afford 2.92 g (96%) of the desired aniline as a light reddish oil. Data for 7-amino-1,2-dihydro-2,2,4,8-tetramethylquinoline: **^{1}H NMR** (400 MHz, $CDCl_3$) 6.89 (d, 1H, *J* = 8.1, 5-H), 6.14 (d, 1H, *J* = 8.2, 6-H), 3.42 (br s, 3H, NH_2, N*H*), 2.87 (ddq, 1H, *J* = 18.7, 12.7, 6.4, 4-H), 1.90 (s, 3H, 8-CH_3), 1.70 and 1.39 (d of ABq, 2H, J_{AB} = 12.8, J_A = 5.6, J_B = 12.5, 3-H), 1.29 (d, 3H, *J* = 6.7, 4-CH_3), 1.27 and 1.16 ppm [2s, 2 x 3H, 2-(CH_3)2].

1,2,3,4-Tetrahydro-2,2,4,10-tetramethyl-6-trifluoromethyl-8-pyridono[5,6-*g*]quinoline. This compound was prepared by General Method 13 (EXAMPLE 147) from 7-amino-1,2,3,4-tetrahydro-2,2,4,8-tetramethylquinoline (2.92 g, 14.3 mmol) and ethyl 4,4,4-trifluoroacetoacetate (3.13 mL, 21.4 mmol, 1.5 equivuiv) to afford 2.04 g (44%) of Compound **409** as a pale fluorescent-yellow solid. Data for Compound **409**: mp 239-40 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) 9.70 (br s, 1H, CON*H*), 7.50 (s, 1H, 5-H), 6.68 (s, 1H, 7-H), 4.13 [br s, 1H, $(CH_3)_2$CN*H*], 3.00 (ddq, 1H, *J* = 12.9, 12.4, 6.3, 4-H), 2.15 (s, 3H, 10-CH_3), 1.83 and 1.46 [dd of ABq, 2H, J_{AB} = 13.0, J_A = 5.3, 1.6 Hz (3-H_{equiv}), J_B = 12.9, 0 Hz (3-H_{ax})], 1.40 (d, 3H, *J* = 6.6, 4-CH_3), 1.36 and 1.25 ppm [2s, 2 x 3H, 2-(CH_3)2]. **^{13}C NMR** (100 MHz, $CDCl_3$) d 162.5, 144.9, 139.1, 137.1, 124.3, 122.7, 120.9, 113.8, 105.7, 101.6, 50.2, 43.5, 31.8, 28.9, 27.6, 20.1, 9.7 ppm. **Anal.** Calcd for $C_{17}H_{19}F_3N_2O$: C, 62.95; H, 5.90; N, 8.64. Found: C, 63.02; H, 6.01; N, 8.48.

EXAMPLE 310

(*R/S*)-1,2,3,4-Tetrahydro-4-methyl-6-trifluoromethyl-8-pyranono[5,6-*g*]quinoline (Compound **410**, structure **33A** of **Scheme XL**, where R^{1-3}=R^6=H, R^4=methyl, R^5=trifluoromethyl)

3-(3-Methoxyanilino)propionic acid. To a oven dried 500 mL rb flask equivuipped with a magnetic stir bar and a water cooled reflux condenser was dissolved anisidine (5 mL, 44.6 mmol) in toluene (70 mL). The stirred solution was heated to reflux and acrylic acid (3.0 mL, 44.1 mmol, 1 equiv) was dripped in over a 10 min period to give a clear colorless solution. After heating at reflux for 3 h the dark red solution was cooled to rt and concentrated *in vacuo* to remove both the unreacted acrylic acid and toluene to give a 6.4 g of a 1:1 mixture of the desired amino acid and anisidine as a red viscous oil. Data for 3-(3-Methoxyanilino)proionic acid: $R_f = 0.1$ (hexanes/EtOAc, 3:1); **^{1}H NMR** (400 MHz, $CDCl_3$) 9.08 (br s, 1 H, NH), 7.28 (d, $J = 4.3$, 1 H), 7.21 (dd, $J = 8.1, 8.1$, 1 H), 7.03 (dd, $J = 1.3, 7.9$, 1 H), 6.67 (dd, $J = 2.3, 8.4$, 1 H).3.80 (s, 3 H), 3.58 (s, 2 H), 2.33 (s, 3 H).

1,2,3,4-Tetrahydro-7-methoxy-4-quinolone. To a oven dried 500 mL rb flask equivuipped with a magnetic stir bar and a N_2 gas inlet, the material obtained above was dissolved in PPA (~150 mL). The resulting red viscous solution was heated at 100°C with constant stirring under a blanket of N_2 for 12 h. The still warm solution was carefully poured over ice (1 L) and while vigorously stirring the iced solution with a metal stir rod the reaction was quenched by slow addition of a sat. K_2CO_3 solution. The near neutral solution was extracted with $CHCl_3$ (5 x 150 mL), washed with brine (2 x 100 mL), dried over Na_2SO_4 and concentrated in vacuo to give an impure solid. The solid was purified by taking up in EtOAc and concentrating the liquor on Celite™ to give a free flowing powder which was purified *via* flash column chromatography (silica gel, CH_2Cl_2 /MeOH, 95:5) to give 1.2 g (62%) of 1,2,3,4-tetrahydro-7-methoxy-4-quinolone as a yellow solid. Data for 1,2,3,4-tetrahydro-7-methoxy-4-quinolone: $R_f = 0.43$ (CH_2Cl_2/MeOH, 95:5); **^{1}H NMR** (400 MHz, $CDCl_3$) 7.79 (d, $J = 8.8$, 1 H), 6.31 (dd, $J = 2.0, 8.9$, 1 H), 6.08 (d, $J = 2.0$, 1 H), 4.54 (br s, 1 H, NH), 3.78 (s, 3 H, OCH3), 3.54 (td, $J = 1.7, 8.0$, 2 H), 2.63 (t, $J = 7.0$, 2 H).

1-*t*-Butoxycarbonyl-1,2,3,4-tetrahydro-7-methoxy-4-quinolone (structure 31A of Scheme XL, where R^{1-3}=H). To a flame dried 250 mL rb flask equivuipped with a magnetic stir bar and a N_2 gas inlet was dissolved 1,2,3,4-tetrahydro-7-methoxy-4-quinolone (1.18 g, 6.67 mmol) and BOC anhydride (2.03 g, 9.33 mmol, 1.33 equiv) in anhydrous THF (60 mL). The solution was cooled to 0°C and N,N-dimethyl-4-aminopyridine (DMAP) (1.30 g, 10.7 mmol, 1.6 equiv) was added with constant stirring. After stirring over N_2 for 16 h the reaction was carefully quenched with 10% $NaHSO_4$ solution (20 mL). The biphasic solution was extracted with EtOAc (3 x 50 mL), washed with brine (2 x 50 mL), dried over Na_2SO_4 and concentrated *in vacuo* to give 1.65 g (90%) of 1-*t*-butoxycarbonyl-1,2,3,4-tetrahydro-7-methoxy-4-quinolone as an off white solid. Data for 1-*t*-butoxycarbonyl-1,2,3,4-tetrahydro-7-methoxy-4-quinolone: R_f = 0.31 (hexanes/EtOAc, 3:1); ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.27 (d, *J* = 1.6, 1 H), 7.06 (d, *J* = 8.5, 1 H), 6.61 (dd, *J* = 2.4, 8.5, 1 H), 3.78 (s, 3 H), 3.71 (t, *J* = 6.0, 2 H), 2.82 (m, 1 H), 2.02 (m, 1 H), 1.57 (m, 1 H), 1.27 (d, *J* = 7.0, 3 H).

(*R/S*)-1-*t*-Butoxycarbonyl-1,2,3,4-tetrahydro-4-hydroxy-4-methyl-7-methoxyquinoline. To a flame dried 250 mL 3-necked rb flask equivuipped with a magnetic stir bar was added Ce(III)Cl·7 H_2O (2.74 g, 7.35 mmol, 2 equiv). The flask was heated in a 140°C oil bath under reduced pressure (~ 1 torr) for 2.5 h. The flask was cooled to rt and slowly filled with N_2 g. The white powder was suspended in dry THF (30 mL), stirred at rt for 1 h and then cooled to -78°C. To the white suspension was added a 1.4 M solution of methyl lithium (MeLi) in Et_2O (5.25 mL, 7.35 mmol, 2 equiv) by syringe. The dark yellow/brown solution stirred at -78°C for 1 h and then 1-*t*-butoxycarbonyl-1,2,3,4-tetrahydro-7-methoxy-4-quinolone dissolved in 3 mL THF was added. The solution stirred at -78 °C for 3 h and was warmed to 0°C for 2 h. The reaction did not go to completion and starting material was observed by TLC (silica gel, hexane/EtOAc, 3:1). The reaction was quenched with H_2O (1 mL) and allowed to warm to rt. The solution was neutralized with sat NH_4Cl solution (5 mL), extracted with EtOAc (3 x 100 mL), washed with brine (1 x 100 mL), dried over Na_2SO_4 and concentrated in vacuo to give a mix of the desired alcohol and starting material. The mixture was taken up in EtOAc and concentrated on Celite™ to give a free flowing powder which was purified *via* flash column chromatography (silica gel, hexanes/EtOAc, 3:1) to give 796 mg (74%) of the desired product as a vicious clear colorless oil. Data for 1-*t*-butoxycarbonyl-1,2,3,4-tetrahydro-4-hydroxy-4-methyl-7-methoxy-quinoline: R_f = 0.20 (hexanes/EtOAc, 3:1); ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.42 (d, *J* = 8.7, 1 H), 7.33 (d, *J* = 2.5, 1 H), 6.66 (dd, *J* = 2.5, 8.6, 1 H), 3.98 (m, 1 H), 3.79 (s, 3 H, OCH_3), 3.61 (m, 1 H), 1.98 (m, 2 H), 1.58 (s, 3 H), 1.53 (s, 9 H).

(*R/S*)-1-*t*-Butoxycarbonyl-1,2,3,4-tetrahydro-4-methyl-7-methoxy-quinoline

To a oven dried 250 mL rb flask equivuipped with a magnetic stir bar was dissolved 1-*t*-butoxycarbonyl-1,2,3,4-tetrahydro-4-hydroxy-4-methyl-7-methoxy-quinoline (44 mg, 150 µmol) in EtOAc (15 mL). The flask was repeatedly evacuated and flushed with N_2 then a catalytic amount of 10% Pd on C (~5 mg) was added. The flask was again evacuated and flushed with N_2 several times and then H_2 was introduced by balloon. The solution was stirred under H_2 for 12 h. The flask was again evacuated and flushed with N_2 several times to remove any residual H_2 and the solution was filtered through a pad of Celite™ and concentrated *in vacuo* to give the desired amine (37.0 mg, 133 µmol, 90% yield) as a clear colorless oil. Data for 1-*t*-butoxycarbonyl-1,2,3,4-tetrahydro-4-methyl-7-methoxy-quinoline: R_f = 0.59 (hexanes/EtOAc, 3:1); ^{1}**H NMR** (400 MHz, $CDCl_3$) 7.28 (d, *J* =2.3, 1 H, Ar-8), 7.07 (d, *J* =8.5, 1 H, Ar-5), 6.61 (dd, *J* =2.5, 8.5, 1 H, Ar-6), 3.78 (s, 3 H, OMe), 3.71 (dd, *J* =6.1, 12.2, 2 H, C2-H), 2,83 (m, 1 H, C4-H), 2.00 (m, 1 H, C3-H), 1.58 (m, 1 H, C3-H), 1.53, (s, 9 H, $(CH_3)_3$), 1.27 (d, *J* =7.0 Hz. 3 H, C4-C$\underline{H}_3$).

(*R/S*)-1,2,3,4-Tetrahydro-4-methyl-7-methoxyquinoline. To a oven dried 250 mL r.b. flask equivuipped with a magnetic stir bar and a N_2 gas inlet was dissolved 1-*t*-butoxycarbonyl-1,2,3,4-tetrahydro-4-methyl-7-methoxy-quinoline (678 mg, 2.44 mmol) in CH_2Cl_2 (15 mL). To the stirred solution was added trifluoroacetic acid (TFA) (2 mL) at rt. The solution stirred under N_2 for 2 h and then quenched with sat $NaHCO_3$ solution (25 mL), extracted with CH_2Cl_2 (3 x 20 mL), washed with brine (1 x 30 mL), dried over Na_2SO_4 and concentrated in vacuo to give 370 mg (77%) of the desired quinoline as a clear colorless oil. Data for 1,2,3,4-tetrahydro-4-methyl-7-methoxyquinoline: R_f = 0.32 (hexanes/EtOAc, 3:1); ^{1}**H NMR** (400 MHz, $CDCl_3$) 6.95 (d, *J* =8.1, 1 H, Ar-5), 6.22 (dd, *J* =2.5, 8.3, 1 H, Ar-6), 6.03 (d, *J* =2,6, 1 H, Ar-8), 3.86 (br s, 1 H, NH), 3.73 (s, 3 H, OMe), 3.28 (m, 2 H, C2-H), 2,85 (m, 1 H, C4-H), 1.95 (m, 1 H, C3-H), 1.64 (m, 1 H, C3-H), 1.25 (d, *J* =6.9, 3H, C4-Me).

(*R/S*)-1,2,3,4-Tetrahydro-7-hydroxy-4-methylquinoline. To a flame dried 25 mL rb flask equivuipped with a magnetic stir bar and a N_2 gas inlet was dissolved 1,2,3,4-tetrahydro-4-